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BONE MATURATION AND CAPILLARY MICROSCOPY AS INDICATORS FOR THE USE OF THYROID IN CHILDHOOD ALLERGY

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WHEN I first became interested in allergy, I believed that allergy could not be viewed from the standpoint of protein hypersensitiveness alone. My conviction has been fortified by many years of experience and today I am more certain than ever that the allergic child must be treated from every aspect as well as for his allergy.

Therefore, besides specific allergenic elimination and specific injection treatment, freedom from stress, adequate mineralization, adequate nutrition, sufficient vitamin intake are all as important as they are in the management of any non-allergenically caused condition. Such measures serve to bring the patient back into physiological balance and permit immunological mechanisms to work under the best possible conditions.

In addition to these measures I should like to consider the appraisal and treatment of thyroid hypofunction. Some children show symptoms of fatigue, poor scholarship, irritability, poor nutrition and susceptibility to infections and are treated month after month with iron tonics, liver injections, multiple vitamins, all without real benefit. It is our impression that such conditions may be due to a form of hypothyroidism and until this basic constitutional deficiency is corrected, other modes of therapy may be only partially effective.

While the determination of basal metabolism rate, blood cholesterol level, plasma bound iodine level and radioactive iodine uptake may be the more sensitive indicators of hypothyroidism, these are nevertheless arduous methods and also impractical as office procedures. This is especially true in the young age group. We do have at hand some simpler methods for detecting hypofunctioning of the thyroid gland, and I pro-

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pose to limit my remarks to two of these, namely, (1) bone maturation and (2) capillary microscopy. First however, we must realize that no single technique is entirely adequate for appraising the child's physical status and secondly that inherent limitations of a procedure should not be obscured by too great enthusiasm for it. The methods of appraising bone maturation and capillary microscopy should merely be regarded as supplements to other measures for a broad evaluation of the physiological balance of the child.

BONE MATURATION

Bone maturation is easily determined and merely requires a fluoroscopic and roentgenographic examination of the bones of the wrist and hand. A roentgenogram of both hands and wrists (anteroposterior) on a single plate is sufficient for assessing skeletal maturation. The x-ray study of the hand and wrists is the most useful single procedure for determining the developmental status of children. Because of the large number of epiphyses that can be seen at one time and assessed, hand films provide a good index to general skeletal development. Rarely is variation in other centers of ossification of significance. An additional advantage is the low cost of this laboratory procedure.

Originally we followed the Todd Atlas in appraising the hand film. A revised and reevaluated edition by Greulich and Pyle[5] was found to have certain advantages over the original. I shall not go into details of appraising bone development for this would require too much time. I would recommend the owning of an Atlas, so that one may become sufficiently familiar with the technique of interpretation to utilize its full potentialities.

Hand films should be repeated at yearly intervals to assess the progress in skeletal maturation.

In the interpretation of the hand film certain factors must be taken into consideration. Environment, for example, plays a role in osseous development. Children of superior homes are normally more mature than those of underprivileged groups. Yet, we did not find that nutrition *per se* was a pertinent factor in skeletal maturation.

There appears to be a positive correlation between height and bone maturation, tall children demonstrate an accelerated development and short children a repressed one. However, short children may show normal or advanced skeletal development because of their early gonadal maturation.

Sex differences must be considered particularly in the prepubescent and pubescent period when the female child shows a growth acceleration of about two years over the male.

We did not find a correlation between serum cholesterol levels (free and total) and skeletal development.

It may be true that severe chronic diseases have a retarding influence

on weight, height and other measurements. However, in a study of the influence of tuberculosis on bone maturation, we[1] recently found the development of the group in general to be slower than that of the Todd standard. This could not be correlated with either the severity of the disease or its duration. We[13] made an analysis of children presenting various grades of rheumatic heart disease and plotted the skeletal against chronological age. No correlation was found to exist between the severity of the disease and the skeletal development. Approximately the same number were retarded, but a significantly greater number were advanced as compared with an unselected control group.

These findings imply that bone maturation is more influenced by factors other than the chronicity or severity of the disease.

There is not yet sufficient evidence that the chronic allergic state *per se* causes deficiencies in skeletal development. We do find patients with bone retardation. However, this does not necessarily predispose the child to allergy, but rather is evidence of a concurrent endocrine disturbance.

My former associate, Dr. A. B. Sussman, and I studied a large number of allergic children from this viewpoint. Our impression was that hypothyroidism in the allergic child does not occur more frequently than in children of the general population. The classical picture of cretinism or childhood myxedema was not observed among our patients. For this reason epiphyseal dysgenesis[16] was not part of the picture observed.

Other symptoms encountered with the retarded bone development were: (a) dry hair or skin, (b) mental sluggishness (though often the children were bright), (c) inability to concentrate, (d) general irritability, (e) behavior problems, (f) flabby panniculus and musculature, (g) fatigability, (h) constipation, (i) obesity (yet often enough thin children were seen), (j) short stature (though a certain percentage were tall), (k) secondary anemia and (l) a relative lymphocytosis in older children.

The presence of several of these abnormalities, coupled with bone retardation add up to a definite syndrome often referred to as masked hypothyroidism, a mild form of thyroid deficiency.[2] As was emphasized by Reilly[10] certain authors still describe only advanced hypothyroidism and disregard the borderline cases.

CAPILLARY MICROSCOPY*

The method for doing capillary microscopy of the nail fold is as follows:

(a) Cedar oil is placed on the nail fold and the finger is held firmly on the microscope platform.

*I should like to express my gratitude to the late Dr. Carl Pototsky who introduced me to the subject of capillary microscopy and who spent many hours teaching me the method which he had employed for more than thirty years in Germany, for what he considered the appraisal of endocrine disturbances in children. I should also like to thank my associate Dr. Samuel Untracht for his translation of material in Müller's[8] and Jaensch's[6] books on the subject from which some of the following observations were gleaned.

(b) The beam of the microscope lamp is focused tangentially on the nail fold.

(c) The area is examined with a microscope using an objective lens of 75 to 100 magnification with a No. 10 ocular.

(d) For the interpretation of one's findings, we have found it useful to make rough sketches for our records.

What one actually visualizes in the microscopic field are the capillaries comprising the arterial branch, the communicating loop and the venous branch and the end arterioles and connecting venules, the subpapillary arteriole network and the venus subpapillary plexus. One can see down to the subpapillar network and, under favorable conditions of extreme transparency, down to the cutaneous network.

The capillary loop itself is a thin tube of endothelial cells surrounded by occasional smooth muscle cells which gradually form a network toward the arteriolar side. The venule side of the capillary loop is wider than the contractile arteriolar side. However, the anatomical boundary between the capillary, arteriole and venule is not distinct or sharp.

The subpapillary plexus is visible only when the skin is unusually transparent. Normally it is vaguely indicated as a network of horizontally placed veins and thinner arterioles.

In order to understand better the several factors of capillary microscopy one might review the changes that transpire from fetal life to birth. The finest terminal capillary loop develops through the embryonic period gradually and progressively from a predominantly horizontal plexus structure to that of a vertical endloop structure. In the course of this development transitional forms appear as pointed arches.

The presence of arched capillaries, termed "archicapillaries" by Jaensch in 1921,[7] indicates a persistence of primitive forms of capillary network long after the fetal period. He explains the presence of such capillary loops, as well as the appearance of many types of hypoplastic forms, as evidence of inhibition of development.

It must be remembered that overmanipulation and irritation of the cuticle may alter the capillary picture. Several fingers should be examined since atypical patterns may be encountered in one finger and not in another.

The capillary patterns may vary with the opinion of the examiner, the presence of gradual transitions which are found in all stages of capillary development, the combination of inhibition of development and pathological states, exogenous influences such as diet, heat and cold, and with acute diseased states.

Jaensch was the first to discover the retarding effect of thyroid hypofunction on the growth of the capillaries. A hypothyroid group of patients was described by him in 1921, based on his examination of cretins and feeble-minded school children. He described a distinctive

capillary pattern of hypothyroidism with or without myxedema. These cases showed inhibition of capillary development, approximating that of the fetal stage. The capillaries are long or short, twisted and whip-formed. Evidence of water retention (also found in adiposity and hydremic states) is manifested. Edema is expressed by abnormal swelling of the papillae which form transparent caps around each terminal loop. The subpapillary plexus is usually evident and these vessels appear engorged.

Capillary microscopy can only serve as an additional method for appraisal of an individual's constitution and it is perhaps best to view capillary patterns as ancillary information.

THYROID THERAPY

Thyroid medication is usually started with gr ¼ in the younger age group and gr ½ in the older child. The patient is checked regularly at least every fortnight. Dosage is gradually increased until the desired effects are obtained in better health and gain in weight. Seldom do we find it necessary to exceed 2 gr of dessicated thyroid daily.

An exceedingly rapid pulse rate and signs of increased irritability are indications for reducing or discontinuing thyroid administration. In a child who is underweight it is wise to reduce the amount of thyroid hormone or to discontinue administration temporarily if he shows a loss of weight. Thyroid may be resumed experimentally in small amounts after a lapse of time. The weight of an obese child will usually fall as the dehydration effects become manifest. If the bone maturation remains retarded, thyroid can be given for several years as long as there is a noticeable response and the child gains in weight and height. We have found that it is wise to discontinue therapy during the hot summer months, and also to stop it intermittently at other periods.

Perhaps the best results are obtained with the eczematous patient. A dry sandpaper-like skin is particularly characteristic, although the moist skin of infectious eczematoid dermatitis may also be observed. Since the skin is a target tissue in hypothyroidism it is believed that the administration of thyroid hormone does aid both the nutrition and resistance of the skin to secondary infection. Such therapy, combined with specific antiallergic and local measures, may help to convert the skin into a more permanently normal tissue. In fact, for many years desiccated thyroid has been used by clinicians in the empirical treatment of eczema.

In infantile eczema the response is so beneficial that thyroid hormone may well act as a specific medication. Such cases are rare for the etiologic basis is probably, in the vast majority of patients, the specific antigenic hypersensitivity. The response of cases resistant to specific treatment is often enhanced when desiccated thyroid is used as an adjuvant.

In respiratory allergies desiccated thyroid apparently aids in reducing

mucosal edema in the respiratory tract. An appreciable number of resistant cases of rhinitis and edema with chronic inflammatory changes and many repeated colds also respond satisfactorily.[9] This is not a new observation since some clinicians assert that some cases of vasomotor rhinitis result from localized myxedematous swelling of the nasal mucosa.

In those children who suffer from recurrent upper respiratory infections, gain weight slowly, and are generally subnormal, the physician finds a serious therapeutic problem taxing his ingenuity. Such children may also be allergic. In cases of this type, where evidence of retarded skeletal development is seen and a typical hypothyroid capillary pattern is observed, the response to thyroid therapy is gratifying. An interesting observation has been that asthmatic children, who belong to this group and in whom asthmatic attacks are at times precipitated by strong winds and undue physical exertion, often respond to thyroid therapy and are prevented from having such future nonspecific episodes.

In our experience, thyroid therapy does not relieve the true allergic attacks of asthma, nor does it lessen the frequency of such attacks. It is our impression that it improves the endurance and general vigor of the patient.

CONCLUSIONS

Studies of the nail fold capillaries and bone retardation are two methods available for rapid and direct appraisal of hypothyroidism.

Capillary microscopy is especially helpful in the study of infants in the early years of life when bone maturation is difficult to appraise and in pubescent children in whom bone development has reached maturity. It is ancillary to a study of osseous development.

Bone studies are best employed in children after the first year and through the prepubital period before epiphyseal fusion is complete. Bone maturation is perhaps the method of choice for it is the most useful single procedure for determining the developmental status of the child.

I doubt that deviations in skeletal growth bear any direct causal relation to allergy.

Although I have implied that a retardation in epiphyseal development and the finding of a typical capillary picture is indicative of a hypothyroid state, this may not be due to lack of thyroid hormone alone. I should like to emphasize that children with retarded bone age often respond to the administration of thyroid substance. Whether such a response is due to supplementation of deficient endocrine substance or whether the beneficial effect is due to its dehydrating, calorigenic, appetite-stimulating or sympathico-tonic effect, I am not prepared to state. The thing that has impressed us over the years is the fact that in the treatment of the allergic child the response to thyroid therapy is a rewarding experience.

REFERENCES

1. Bashe, W. J., Jr., and Ratner, Bret.: Bone development in children with tuberculosis. I. Maturation determined by the Todd method. Unpublished.
2. Dorff, George B.: Masked hypothyroidism in children. J. Pediat., 6:788, 1935.
3. Engelbach, Wm., and McMahon, A.: Osseous development in endocrine disorders. Endocrinology, 8:1, 1924.
4. Finkler, R. S.; Furst, N. J., and Klein, M.: Clinical and roentgenological study of the effects of hormonal therapy on bone growth. Radiology, 43:346, 1944.
5. Greulich, W. W., and Pyle, S. I.: Radiographic Atlas of Skeletal Development of the Hand and Wrist. Stanford: Stanford University Press, 1950.
6. Jaensch, Walther: Die Hautkapillarmikroskopie. Halle: Carl Marhold, 1929.
7. Jaensch, W.: Psychophysical Constitutional Types. München. med. Wchnschr., 68:1101, 1921.
8. Müller, Otfried: Die feinsten Blutgefässe des Menschen in gesunden und kranken Tagen. Stuttgart: Ferdinand Enke, Vol. I, 1937, Vol. II, 1939.
9. Proetz, A. W.: The thyroid and the nose. Ann. Otol. Rhin. & Laryng., 56:328, 1947; Further observations of the effects of thyroid insufficiency on the nasal mucosa. Laryngoscope, 60:627, 1950.
10. Reilly, Wm. A.: Hypothyroidism in childhood. J.A.M.A., 146:234, 1951.
11. Rotch, T. M.: Chronologic and anatomic age in early life. J.A.M.A., 51:1197, 1908.
12. Shelton, E. K.: Familial hypothyroidism. Endocrinology, 15:297, 1931; Osseous development as an index of metabolism. Radiology, 20:241, 1933.
13. Sussman, A. B., and Ratner, Bret: Unpublished.
14. Todd, T. W.: Atlas of Skeletal Maturation. St. Louis: The C. V. Mosby Company, 1937.
15. Topper, A.: The effect of thyroid therapy on underdeveloped children. Am. J. Dis. Child., 41:1289, 1931.
16. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield: Chas. C Thomas, 1950.
17. Wilkins, L., and Fleischmann, W.: The diagnosis of hypothyroidism in childhood. J.A.M.A., 116:2459, 1941.

50 East 78th Street

SMOKING AND ASTHMA

No patient who has asthma should smoke. Smoke of any type is irritating, not soothing, to mucous membranes. Smoking induces cough, bronchitis and bronchospasm, which are nature's warning to avoid or to expel the irritating effects of smoke. Likewise, any temporary benefit that patients derive from smoking so-called asthma cigarettes or burning powders which contain stramonium or nitrates, is nullified by the deleterious effect of the smoke itself, which aggravates the patients' bronchitis. All patients with asthma have some degree of bronchitis. Most asthmatic people have considerable bronchitis, as evidenced by inflamed, red, swollen, mucous membranes, covered with protecting mucus, and associated with some degree of bronchospasm. Such inflamed membranes are extremely sensitive to such irritants as dust, smoke, fumes, cold air, and strong odors.

Smoking is one of the most common sources of bronchial irritation, and invariably increases cough and asthma when continued any length of time. No patient with asthma should irritate his inflamed membranes with smoke, any more than a patient with conjunctivitis should blow smoke in his eyes. . . If a patient has asthma, it is not enough to reduce smoking; it must be completely stopped.—G. A. PETERS, L. E. PRICKMAN, G. A. KOELSCHE, and H. M. CARRYER, *Proc. Staff Meet. Mayo Clinic*, 27: 329, 1952.

GASTROINTESTINAL ALLERGY AND THE CELIAC SYNDROME WITH PARTICULAR REFERENCE TO ALLERGY TO COW'S MILK

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IN 1942 one of us (RHK) emphasized food allergy as a causative factor in certain cases of the celiac syndrome and suggested its inclusion in the etiologic classification of this syndrome.[11]

After a period of over ten years, we again wish to emphasize the importance of gastrointestinal allergy in the celiac syndrome. It has been our experience to have observed an increasing number of children with food allergy, several of whom had been hospitalized for idiopathic celiac disease, where the simple expedient of careful history, observation and proper management would have eliminated a great deal of anxiety on the part of the parents, unnecessary expense due to many involved laboratory procedures including gastrointestinal x-rays, chemical analysis of the stools and duodenal contents, and intestinal absorption tests.

Since our original report, Anderson[3] has reviewed her experience and now includes gastrointestinal allergy in her etiologic classification of the celiac syndrome.[4] Among eighty-one records of her original series, fourteen have been found with a history of allergy as defined by the presence of asthma, hay fever, severe eczema or proved gastrointestinal allergy—of these, nine were considered to have major allergy. She believes that this incidence is not significantly greater than has sometimes been estimated for the general populace. However, she admits that occasional cases presenting the celiac syndrome permit the interpretation that, in some instances, celiac disease is due to intestinal allergy.[4] McKhann and his associates point out that some outspoken cases of gastrointestinal allergy showed symptoms very close to those of celiac disease. Furthermore, in certain other types of allergic conditions they observed interference with absorption of food substances similar to that which occurs in celiac disease.[15] They concluded that, although an association might exist between allergy and the celiac syndrome, it is possible that the symptomatology of gastrointestinal allergy may simulate that of celiac disease, although the latter diagnosis is finally ruled out. Block[5] recently emphasized the allergic factor in the celiac syndrome and discussed the importance of various food allergens. In discussing celiac disease, McCreary and his colleagues[14] recently stated "it has become evident that three separate entities can be split off the main group of cases manifesting celiac symptoms. 1—celiac syndrome due to chronic or repeated infection; 2—

From the Sarah Morris Hospital for Children, Michael Reese Hospital, Chicago.
Presented at the Round Table on Pediatric Allergy, The American College of Allergists, Chicago, Illinois, April 28, 1953.

fibrocystic disease of the pancreas, and 3—food allergy." They state that a small number of cases are observed where local allergic response on the part of the intestine may be postulated, the most common allergen being cow's milk. "The diagnosis may be established by the spectacular improvement following the institution of a milk-free diet—and probably every case should be given a therapeutic trial for two or three weeks off cow's milk products. Where there is a strong family history of allergy, investigation for other possible allergens may be indicated."

In discussing the presentation of Charlotte M. Anderson and her co-workers on gastrointestinal studies and the effect of dietary wheat flour in celiac disease,[1] Shwachman recently stated "one may also speculate as to whether we are dealing with an allergic factor involving the gastrointestinal mucosa. Some workers have considered an allergic reaction one of the possible etiologic mechanisms of idiopathic celiac disease."[17]

It is not our intent to label celiac disease as an allergic disease *per se*, but to stress allergy as an important factor in the production of the syndrome in certain cases. In our experience, *cow's milk* is the most frequently encountered allergen responsible for allergic diarrhea, and our thirty-six cases of chronic, recurrent diarrhea form the basis for this report (Table I). Our criteria for the diagnosis of the celiac syndrome are those described by Anderson.[4] "The celiac syndrome is a clinical picture characterized by chronic indigestion and failure to gain weight normally during infancy and childhood. The indigestion results in the excretion of bulky, foul stools containing undigested starch, fat and visible food fragments at some time during the course of the disease. There is chronic or intermittent diarrhea with intervening periods of constipation. The patient develops a 'celiac habitus' with protuberant abdomen, weak, flabby muscles and some degree of wasting. The term 'celiac syndrome' is used in preference to 'celiac disease' because the clinical picture may result from a variety of causes." Of our thirty-six cases of diarrhea, eleven (30.5 per cent) presented the clinical picture of the celiac syndrome described above.

There were nineteen boys and seventeen girls. The age at onset of the diarrhea is indicated in Table II.

In seventeen or 47.2 per cent of the thirty-six cases, diarrhea began during the first three months of life. Of these, four or 23.5 per cent developed the celiac syndrome. Nine or 53 per cent of the seventeen patients developed symptoms during the first week of life, whereas only two of these subsequently developed the celiac syndrome. All of these nine infants were fed exclusively cow's milk formulae.

Of the thirty-six cases, in eighteen or 50 per cent a history of some form of allergy was elicited in the immediate family, parents or siblings. Eighteen or 50 per cent of the infants had some manifestation of allergy other than diarrhea, viz., allergic dermatoses, eczema, asthma, so-called allergic rhinitis, hay fever, et cetera. Among the eleven cases of the celiac

TABLE I. GASTROINTESTINAL COW'S MILK ALLERGY
Summary of Thirty-six Cases of Chronic or Recurrent Diarrhea.

	Sex	Present Age	Age Onset of Diarrhea	Age Milk Removed From Diet	Duration Off Cow's Milk	Age Cow's Milk Tolerated	Family History Allergy	Other Allergies of Patient	Previous Treatment Antibiotics and/or Sulfa	Remarks
1.	M	5 yrs.	17 mos.	20 mos.	22 mos.	3½ yrs.	+	+	+	Hospitalized for celiac syndrome
2.	F	20 mos.	1st wk.	2 wks.	9½ mos.	10 jos.				
3.	F	2 yrs.	1 mo.	2 mos.	16 mos.	18 mos.		+		
4.	F	2¾ yrs.	21 mos.	?	?	?	+	+	+	
5.	F	5 yrs.	1st wk.	15 mos.	21 mos.	3 yrs.				
6.	M	2½ yrs.	2 mos.	3 mos.	21 mos.	2 yrs.	+	+		Hospitalized for celiac syndrome; Sister idiopathic celiac disease
7.	M	2 yrs.	5 mos.	?	?	?	+			
8.	F	20 mos.	10 mos.	19 mos.	?	?			+	
9.	M	5 yrs.	1st wk.	17 mos.	Still off, 43 mos.		+	+	+	
10.	F	4½ yrs.	2 wks.	24 mos.	12 mos.	3 yrs.				
11.	M	2 yrs.	12 mos.	?	?	?	+			
12.	M	3 yrs.	11 mos.	12 mos.	18 mos.	2½ yrs.	+			
13.	F	4½ yrs.	14 mos.	30 mos.	6 mos.	3 yrs.				
14.	F	15 mos.	5½ mos.	9½ mos.	Still off, 5½ mos.		+		+	Hospitalized for celiac syndrome
15.	F	3½ yrs.	5 mos.	5½ mos.	14 mos.	19½ mos.	+	+		
16.	F	2¼ yrs.	1st wk.	10½ mos.	13½ mos.	2 yrs.	+			Hospitalized for celiac syndrome
17.	F	8 mos.	1st wk.	2½ mos.	Still off, 5½ mos.		+		+	
18.	F	8 mos.	3 mos.	?	?	?				
19.	M	1 yr.	2½ mos.	3 mos.	Still off, 9 mos.					
20.	M	2½ yrs.	1st wk.	3 wks.	Still off, 29 mos.		+	+	+	
21.	F	2½ yrs.	12 mos.	19 mos.	Still off, 11 mos.				+	
22.	M	3½ yrs.	1st wk.	24 mos.	Still off, 18 mos.		+	+		
23.	M	4 yrs.	1st wk.	17 mos.				+		
24.	M	4½ yrs.	10 mos.	14 mos.				+		Hospitalized for celiac syndrome
25.	M	3¾ yrs.	2 mos.	3 mos.	27 mos.	2½ yrs.		+	+	Hospitalized for celiac syndrome
26.	M	2½ yrs.	15 mos.	22 mos.	Still off, 8 mos.			+	+	
27.	M	3 yrs.	1st wk.	3 mos.	33 mos.	3 yrs.	+	+		
28.	F	9 yrs.	12 mos.	24 mos.	12 mos.	3 yrs.	+	+	+	
29.	M	4½ yrs.	2 mos.	17 mos.	31 mos.	3-2/12 yrs.				
30.	F	3 yrs.	11 mos.	20 mos.	?	?			+	Patient lost
31.	M	3 yrs.	18 mos.	19 mos.	11 mos.	2½ yrs.	+	+	+	Hospitalized for celiac syndrome
32.	F	2½ yrs.	18 mos.	21 mos.	3 mos.	2 yrs.				
33.	M	11 yrs.	12 mos.	19 mos.	17 mos.	3 yrs.	+	+		Hospitalized for celiac syndrome
34.	M	14 yrs.	10 mos.	18 mos.	18 mos.	3 yrs.		+		Hospitalized for celiac syndrome
35.	F	14½ yrs.	5 mos.	18 mos.	42 mos.	5 yrs.	+	+		Hospitalized for celiac syndrome
36.	M	3 mos.	9 wks.	2½ mos.	Still off, 2 mos.					Hospitalized for celiac syndrome

syndrome in this group of thirty-six patients, eight or 72.7 per cent had a family history of allergy and some other manifestation of allergy. In some cases these allergies preceded the diarrhea, in others they were co-existent, and in others they developed following recovery from the diarrhea. In

TABLE II. AGE ONSET DIARRHEA—36 CASES

Age Onset Diarrhea	Celiac Syndrome	Diarrhea Without Celiac Syndrome
Birth to 3 months	4	13
4 to 6 months	2	2
7 to 12 months	3	6
13 to 24 months	2	4
	11 (30.5%)	25 (69.5%)

the majority of instances these conditions were caused by allergens other than cow's milk; namely, other foods, inhalants or contact irritants. However, some of the infants who had recovered from the diarrhea following withdrawal of cow's milk, developed other allergy on re-introduction of cow's milk into the diet at a later date.

Of the thirty-six patients, eleven had been hospitalized with a tentative diagnosis of the celiac syndrome. All had stool cultures for pathogens and analysis of the stools for fat, starch and trypsin. A few had had duodenal aspiration for determination of viscosity and trypsin. Some had had gastrointestinal x-ray studies. A number of patients had had stool cultures and gastrointestinal x-rays as outpatients. In none of these cases was the diagnosis of idiopathic celiac disease or fibrocystic disease of the pancreas confirmed, and in no case was the syndrome caused by intestinal pathogens.

Of the thirty-six patients, nineteen required elimination of cow's milk from the diet for periods ranging from three to forty-two months; an average of 18.3 months. These nineteen infants were able to tolerate cow's milk without diarrhea or other gastrointestinal symptoms at the age of approximately two and a half to three years. Nine patients are still under observation free of gastrointestinal symptoms while on a milk-free diet for periods ranging from two to forty-three months with an average of 25.7 months. For various reasons we have been unable to follow the course of the remaining eight patients. Of the eleven cases of celiac syndrome, eight cases required elimination of cow's milk for a period of eleven to forty-two months with an average of 21.4 months. These infants were able to tolerate cow's milk at an average age of three years with no recurrence of the celiac syndrome. Two patients are still under observation off of cow's milk five and a half and two months, respectively. One is included among the eight cases that we were unable to follow.

In addition to many changes in formula and symptomatic treatment for the diarrhea, thirteen (36.1 per cent) of the thirty-six infants had received various antibiotics and/or sulfonamides singly or in combination.

Some of the patients were treated empirically at home, others were treated at home or in the hospital after questionable intestinal pathogens had been cultured from the stools. These organisms included *Pseudomonas aeruginosa, Proteus morganii* and *mirabilis, Paracolon* and *B. coli.* Little or no improvement occurred in the majority of cases and any improvement was temporary, with return of symptoms on cessation of treatment.

DISCUSSION

Although the classical celiac syndrome as described by Anderson above usually presents no diagnostic problem, nevertheless, in the early stages, the symptoms and clinical findings may not be obvious and may resemble those seen in chronic intermittent diarrhea due to other causes. Often it may be necessary to exclude fibrocystic disease of the pancreas, and celiac syndrome arising secondary to other gastrointestinal disease: dysentery, tuberculosis, parasitic disease, et cetera, and gastrointestinal allergy.

It is unfortunate that too often only classical celiac disease is kept in mind. This picture is present only in well-developed or in neglected cases. Early in the disease, the large, foul, foamy stools may not be present, the stools may be watery, often mucoid, and vary from pale cream to greenish yellow[7]—not characteristic of any specific syndrome. The number of stools is not significant and may vary from two or three to a considerable number in a period of twenty-four hours. In idiopathic celiac disease, Anderson states, "as a rule the infant is normal at birth but in the majority of cases, diarrhea or vomiting and poor weight gain appear before the ninth month." In half of her cases "the first digestive symptoms appeared between one and twelve weeks of age leading to numerous changes of formula." In our eleven allergic infants with the celiac syndrome, 23.5 per cent developed their symptoms within the first three months of life.

The eleven infants with the celiac syndrome had been hospitalized for study. These were cases unrecognized as allergic disease and treated for weeks and months by many changes in diet, often the "celiac diet"—high protein, low fat and low starch with particular emphasis on low fat cow's milk. A typical history in all cases revealed many changes in cow's milk formula, and often goat's milk. In most of the cases fruits, vegetables and vitamins had been eliminated from the diet at various times in an attempt to control the diarrhea. Many had received paregoric, belladonna, kaolin-pectin compounds, sulfonamides or antibiotics or both in addition to dietary changes. Improvement occurred infrequently for short periods of time, often not at all, and recurrence of symptoms was common after discontinuing medication. Often a change of physician with subsequent change of treatment and diet prolonged the disease. In all of these cases laboratory studies contributed no positive evidence for idiopathic celiac disease, fibrocystic disease of the pancreas, or enteric infection. These

negative reports are not surprising for several reasons: examination of the stool for fat is useful only if the fat content of the feces is found to be markedly elevated.[10] Although idiopathic celiac disease is the principal disease in which steatorrhea is found, it can occur in other diseases as well. In idiopathic celiac disease, the occurrence of steatorrhea is a variable which depends on the severity of the diarrhea at the moment when a specimen for examination is passed.[2] A finding of normal fat content in the stool in no way excludes a diagnosis of idiopathic celiac disease. The discovery of starch granules in the stool is of dubious significance because "the variations are so great that in most instances, the presence of intracellular starch is of little diagnostic importance."[4] Although extracellular starch is usually present in idiopathic celiac disease, it may be absent under various circumstances; its presence may depend on the intensity of the diarrhea at the time of the collection of the samples.[10]. If there are frequent, loose movements, the intestinal passage time is short, and many items of ingested material may be found in the stool. Moreover, "extracellular starch granules are absent or few in number unless cereal starch has been fed."[4]

Stool culture in many of our cases revealed a variety of questionable intestinal pathogens such as *B. coli, Paracolon, Proteus morganii, mirabilis* and *Ps. aeruginosa* for which sulfonamides and/or antibiotics had been administered with little or no improvement in the diarrhea. It is our opinion that the presence of these organisms in the stools were unrelated to the diarrhea in any of our cases.

A few cases showed an increase in blood eosinophils, and a few showed eosinophils in mucus eliminated with the stools[16]—both suggestive of an allergic etiology. However, these observations usually were not helpful in establishing a diagnosis.

Of extreme importance, from a diagnostic standpoint, is the allergic history that is often present. Among the eleven cases of the celiac syndrome, eight or 72.7 per cent of the patients had a positive family history for allergy. Eight (72.7 per cent) had experienced some other form of allergy such as, allergic dermatoses, asthma, hay fever, et cetera, at some time from birth up to the development of, during, or after, recovery from the celiac syndrome. Some of these symptoms are common in milk allergy as recently reported by Clein.[6] In many of these cases, a careful history indicated that the gastrointestinal symptoms occurred with the addition of new foods to the diet, usually cow's milk. Some, in early infancy, had been described as colicy, irritable, "vomiters," and many had passed curdy, greenish and mucoid stools. Although such stools are often an early allergic manifestation they may be present in true celiac disease.[15]

It is stated that the child with allergic diarrhea is well nourished and appears healthy.[14] However, if the diarrhea is persistent or of long duration, anorexia occurs, the infant becomes sallow, anemic and may appear wasted and the abdomen becomes distended. This we observed in all

of our eleven patients and the clinical picture resembled true celiac disease. Clein[6] recently stated that several of his 140 cases of cow's milk allergy had previously been diagnosed as celiac disease and two infants later developed celiac disease.

From the standpoint of actual diagnosis, we believe that the problem is not complex. First of all, an awareness of an allergic etiology based on a family history or other manifestations of allergy by the child is important. Secondly, and most important, is the response to complete elimination of cow's milk and all dairy products from the diet. In any case of diarrhea that has not responded to simple dietary adjustments and symptomatic treatment in a period of two to three weeks and where there is no obvious evidence of enteral or parenteral infection, cow's milk and all dairy products should be eliminated from the diet. In cases of milk allergy the response is often dramatic, the diarrhea disappears in from two to three days and general clinical improvement with weight gain is rapid. Occasionally it may take a little longer, until adequate time for the offending milk to be eliminated fully from the system. We further believe that a great deal of time is saved by complete elimination of all cow's milk substitutes for a period of five to seven days. During the trial period fluids may be maintained by water, tea, broth or cereal water, and subsequently fruit juices and milk substitutes such as soy bean and "meat milk"[7,8] may be tried. Also, it is well to remember that since most infants allergic to cow's milk are often sensitive to goat's milk, all animal milk should be avoided.[6] Multiple dispersable and water soluble vitamins and minerals, should be added to the diet. A basic diet for older infants and children consisting of the aforementioned fluids, in addition to cereal, dry toast, crackers, jelly, strained meats, individual strained vegetables and fruits, gelatin and other puddings prepared without milk may be given. It has been our experience that after a period of several months, to a year or more, when the infant has reached a good state of nutrition with consistently normal stools, re-introduction of cow's milk may be attempted in small amounts, gradually increasing to tolerance. A relapse is an indication for immediate withdrawal of the milk. We have found that most of these infants are able to tolerate small to moderate amounts of boiled cow's milk at approximately two and a half to three years of age. Clein[6] states that many of the babies in his series "outgrew" their allergy to cow's milk within three to four months. However, 15 per cent of his patients were still unable to tolerate milk from one to five years later.

It is interesting that many of these children developed other forms of allergy such as hay fever, asthma, allergic rhinitis and eczema, after they had recovered from the diarrhea with elimination of cow's milk. Others developed these various allergic manifestations without gastrointestinal symptoms on re-introduction of cow's milk later. This is in agreement with Clein's remarks that almost every one of these infants with gastro-

intestinal allergy will have symptoms of major allergy as he grows older.[6]

Insofar as skin testing is concerned, we are in agreement with Clein that it is not a dependable method for the determination of food allergy.[6] Matheson *et al* have shown that the skin of newborn infants reacts to certain allergens, particularly egg white[12] but also agree that as a means of determining cow's milk sensitivity, skin testing is unreliable.[13]

SUMMARY AND CONCLUSIONS

The importance of gastrointestinal food allergy in the etiology of infantile diarrhea is re-emphasized. Eleven of thirty-six cases clinically presented the celiac syndrome. Cow's milk was the principal offending allergen.

In almost one-half of thirty-six cases studied, gastrointestinal symptoms, particularly diarrhea, began during the first three months of life. Of the eleven cases of celiac syndrome four or 23.5 per cent began during the first three months of life.

A family history of allergy and other allergic manifestations were present in 50 per cent of the thirty-six cases of diarrhea; 72.7 per cent of those with the celiac syndrome gave a family history of allergy and showed other manifestations of allergy.

Many of the infants were able to consume cow's milk without diarrhea after abstinence for periods of three to forty-two months (average 18.3 months) usually at the age of two and a half to three years. Of the eleven cases of the celiac syndrome, eight required elimination of cow's milk from eleven to forty-two months (average 21.4 months). These were able to tolerate cow's milk without recurrence of the celiac syndrome at an average age of three years.

A diagnosis of gastrointestinal allergy due to cow's milk can be made when gastrointestinal symptoms completely disappear on eliminating cow's milk and all dairy products from the diet and a prompt recurrence of these symptoms are manifested on re-introduction of these foods. Response to complete withdrawal of milk is usually dramatic, with improvement in two to three days.

REFERENCES

1. Anderson, Charlotte M.; Frazer, A. C.; French, J. M.; Serrard, J. W.; Sammons, H. G., and Smellie, J. M.: Celiac disease: gastrointestinal studies and effect of dietary wheat flour. Lancet, 1:836 (Apr. 26) 1952.
2. Anderson, Dorothy H.: Celiac syndrome. Determination of fat in feces, reliability of two chemical methods and microscopic estimate: excretion of feces and fecal fat in normal children. Am. J. Dis. Child., 69:141, 1945.
3. Anderson, Dorothy H.: Celiac syndrome. VI. The relationship of celiac disease, starch intolerance and steatorrhea. J. Pediat., 30:564, 1947.
4. Anderson, Dorothy H., and di Saut'agnese, Paul A.: The Celiac Syndrome. Brenneman's Practice of Pediatrics. Vol. 1. Chapter 29, p. 33.

5. Block, Harry: Celiac syndrome due to gastrointestinal allergy. Arch. Pediat., 66:54, 1949.
6. Clein, Norman W.: Cow's milk allergy in infants. Ann. Allergy, 9:195, 1951.
7. Glaser, Jerome: The use of strained meats as the protein basis for milk substitutes in the treatment of milk allergy. New York J. Med., 43:2399 (Dec. 15) 1943.
8. Glaser, Jerome and Johnstone, Douglas E.: The use of meat as the source of protein in milk substitutes in allergic gastrointestinal disorders of early infancy. Ann. Allergy, 10:564 (Sept.-Oct.) 1952.
9. Haas, Sidney, V., and Haas, Merrill, P.: Diagnosis and treatment of celiac disease. Post-Grad. M., 7:239 (April) 1950.
10. Haas, S. V., and Haas, M. P.: Management of Celiac Disease. p. 119. Philadelphia: J. P. Lippincott Co., 1951.
11. Kunstadter, Ralph H.: Gastrointestinal allergy and the celiac syndrome. J. Pediat., 21:193, 1942.
12. Matheson, A.; Nierenberg, M., and Greengard, J.: Reactivity of the skin of the newborn infant. Pediatrics, 10:181 (Aug.) 1952.
13. Matheson, A.: Personal Communication.
14. McCreary, J. F.; Abbott, Vivien; Pocock, Ruth, and Brown, Alan: The celiac syndrome. Canad. M. A. J., 64:424, 1951.
15. McKhann, Charles F.; Spencer, S., and Meseive, Emily R.: An association of gastrointestinal allergy with the celiac syndrome. J. Pediat., 22:362, 1943.
16. Rosenblum, Arthur H., and Rosenblum, Philip: Gastrointestinal allergy in infancy: significance of eosinophils in the stools. Pediatrics, 9:311 (Mar.) 1952.
17. Shwachman, Harry: Year Book of Pediatrics. p. 173. Chicago: Year Book Publishers Co., 1952.

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EDUCATIONAL STANDARDS IN MEDICINE

All physicians who are interested in maintaining high educational standards in Medicine should read "New Challenges to Medical Education" by Willard C. Rappleye, M.D., reprinted from the Report of the Dean of the Faculty of Medicine of Columbia University for the academic year ending June 30, 1953. There are approximately 1700 approved internships and 3940 approved residencies in the State of New York. This represents about one-sixth of the approved internships and approximately one-fifth of all of the residencies in the United States. Therefore, the Brydges Act, which went into effect July 1, 1953, is of national as well as local significance. It is a direct step backward in medical education.

FREQUENCY OF POLIOMYELITIS IN PATIENTS RECEIVING POLLEN EXTRACT INJECTIONS

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THE INFLUENCE of prior injections of immunizing agents on poliomyelitis continues to be of concern.[1] In view of the early view that specific antigens employed in the therapy of pollen hay fever and asthma might influence the poliomyelitis syndrome, a survey was undertaken to determine if injections of pollen extracts led either to an increased frequency of poliomyelitis or to an altered pattern of the disease. Through the co-operation of the American College of Allergists (which also paid all expenses) all the allergists affiliated with both national societies received a letter in February, 1952, embodying the following questions:

1. The number of patients I have taken care of this past summer who have received pollen injection therapy is .....
2. The number of cases of Infantile Paralysis that I have observed in this group is .....

Over 800 allergists responded with data covering 153,749 patients who received pollen therapy prior to and during the summer of 1951. In Table I is given the number of cases for each State followed by the number of cases of poliomyelitis observed in the patients receiving pollen therapy. The total number of poliomyelitis cases reported in this series was twenty-nine. This is about the anticipated rate and indicated that pollen therapy as commonly employed does not increase the incidence of poliomyelitis. Figure 1 visualizes the distribution of cases and poliomyelitis incidence on a map of the United States.

An attempt was made to ascertain by secondary questionnaire to those physicians reporting cases, whether the site of injection influenced the location of paralysis, if any. The series was too small to draw any definitely negative conclusions. If anything was to be concluded, however, the injections apparently did not increase paralysis or increase the frequency of bulbar paralysis. But as mentioned, this is too small a series for a significant study of this type.

The foregoing data were reported by the writer at the meeting of the Public Health Service in Washington, D. C., March 14, 1952.

SUMMARY

Twenty-nine cases of poliomyelitis were reported by allergists during a nationwide survey of 153,749 patients receiving preseasonal and seasonal

This research was aided by a grant from the American College of Allergists, Minneapolis, Minnesota.

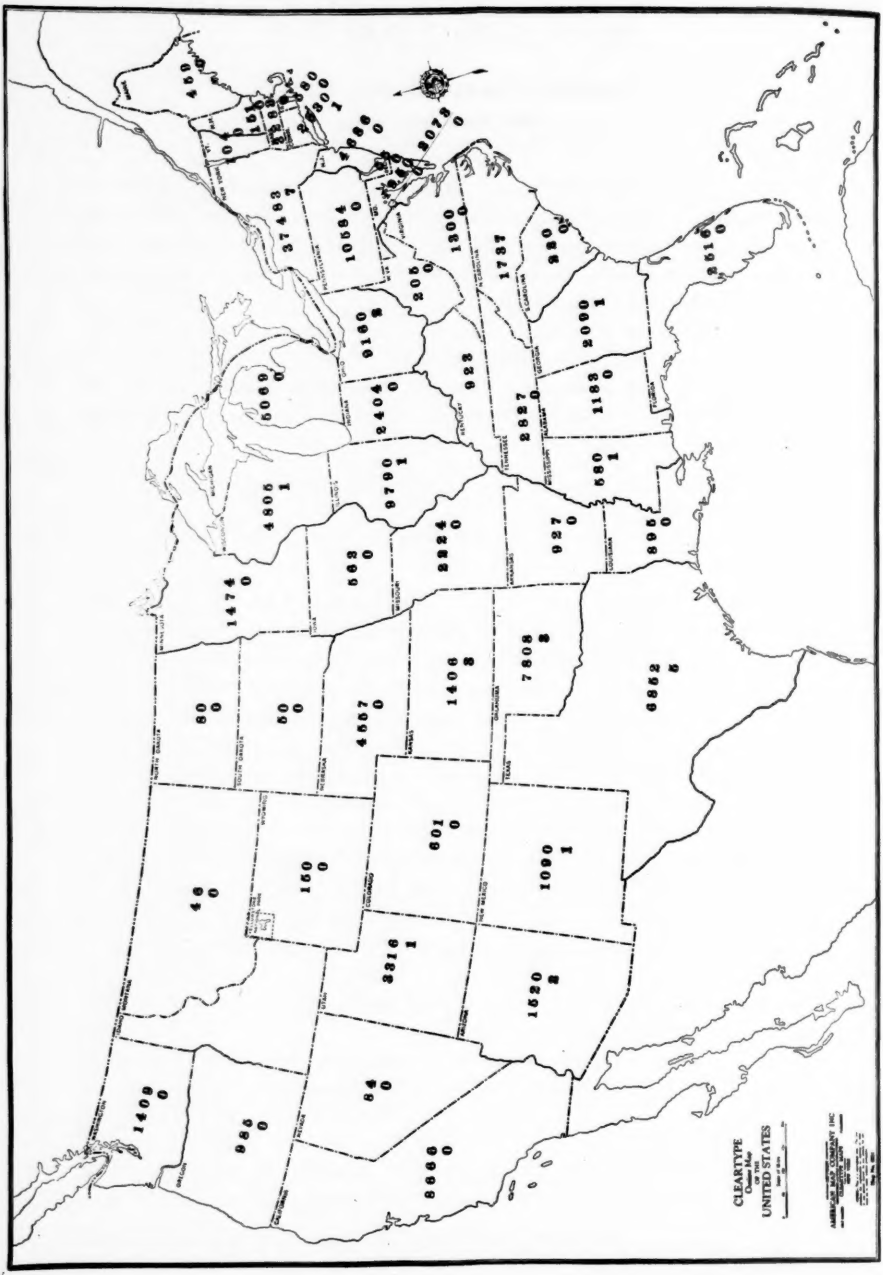

Fig. 1. Frequency of poliomyelitis in patients receiving pollen extract injections.

TABLE I.

State	Patients Received Pollen Therapy	Polio
Alabama	1183	None
Arizona	1520	2
Arkansas	927	None
California	8666	None
Connecticut	2830	1
Colorado	601	None
Delaware	55	None
Florida	2516	None
Georgia	2090	1
Illinois	9790	1
Indiana	2404	None
Iowa	562	None
Kansas	1406	3
Kentucky	923	None
Louisiana	895	None
Maine	459	None
Maryland	1950	None
Massachusetts	3283	None
Michigan	5069	None
Minnesota	1474	None
Mississippi	580	1
Missouri	2224	None
Montana	46	None
Nebraska	4557	None
Nevada	84	None
New Hampshire	151	None
New Jersey	4686	None
New Mexico	1090	1
New York	37483	7
North Carolina	1737	None
North Dakota	80	None
Ohio	9160	2
Oklahoma	7808	3
Oregon	985	None
Pennsylvania	10584	None
Rhode Island	580	None
South Carolina	220	None
South Dakota	50	None
Tennessee	2827	None
Texas	6852	5
Utah	3316	1
Vermont	104	None
Virginia	1300	None
Washington	1409	None
District of Columbia	2073	None
West Virginia	205	None
Wisconsin	4805	1
Wyoming	150	None
Total	153,749 patients	Total 29 patients

Fig. 1. Frequency of poliomyelitis in patients receiving pollen extract injections.

pollen therapy. This is approximately the anticipated rate. Immunization by pollen extracts does not increase the incidence of infantile paralysis. This type of immunization as indicated by the small series reported apparently does not increase bulbar paralysis or affect the location of paralysis when it occurs.

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REFERENCE

1. Greenberg, M., and Abramson, H.: The influence of prior injections of immunizing agents and of penicillin on the occurrence and severity of poliomyelitis. New York State J. Med., 52:2624, 1952.

PSYCHOTHERAPY IN ACUTE ATTACKS OF BRONCHIAL ASTHMA

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WHEN THE asthmatic patient brings his disturbed physiology to the doctor, he inevitably brings along with him his disturbed emotions. He cannot bring one without the other. To the patient, each act of the doctor—from the prescribing of a tablet to the giving of an intravenous injection, is freighted with emotional meaning. Wittingly or unwittingly, therefore, the doctor is involved in the patient's emotional life. When the physician treats the patient medically, he cannot help treating him as well psychologically.

Just as it is important to know the physiological dynamics behind the physical disturbances in the asthmatic patient, so it is important to know the psychological dynamics behind the emotional disturbances which invariably accompany them. When the doctor is aware of these and takes them into account, he can more skillfully manage the diagnosis and treatment.

In approaching a physical disturbance, the physician is often aware of the areas of the body in which to look for its causes. He can therefore go directly to these areas in search of the trouble.

Fortunately, today the emotional disturbances can be approached just as directly. There are also certain areas of the psyche to which the doctor can immediately turn.

One of these areas, and one of prime importance in setting off the asthmatic patient's symptoms, is the patient's hunger for affection. Although the asthmatic patient often hides this hunger for affection behind a façade of bravado or aggressiveness, he is always hoping for more affection than he has. He is dependent and clinging, holding on to the fantasy always that the love he wants is just around the corner. He looks for it demandingly, importuningly if he dares. No matter how old he is, he still seeks from a parent, or from a person on whom he pins the picture of a parent, the emotional nourishment which a warm, acceptant parent would give.

A second emotional area of prime importance in the asthmatic patient is his fear that the emotional food he craves will not be forthcoming, or that the "little" he has will be taken away. And yet despite his dependency and clinging he has difficulty really in trusting or relying on anyone. He fears that he will be rejected just as he has feared, either on a realistic or an imaginary basis earlier in his life, that he was rejected in particular by his mother.

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Because of the real or fantasied deprivation of love; because of the real or fantasied rejection, the asthmatic has a great deal of hidden anger. This is the third area of emotions which must be taken into account. Regardless of age, he continues to be angry at a parent or at a person on whom he has pinned the picture of the parent. Again he he may hide his feelings behind a façade. He may appear compliant, reasonable and appreciative. But behind these, nonetheless, he is angry.

Although the force of his anger may not be great, still he imagines that if he shows it, he runs the risk of losing his chance to gain the love he still must seek. He is desperately anxious and afraid of the hostility he feels. He seeks safety in repression. Anxiety with its attendant product, repression, is then the fourth area of the emotions which the doctor must take into account.

In seeking the psychological factors present in the acute attack of asthma, the doctor can immediately turn his attention to these four areas of the patient's psyche—viz: hunger for affection, fear of losing what affection he has, anger at the person from whom he wants additional affection, and anxiety over exposing this anger.

In the acute attack, the asthmatic closes his bronchial tubes as though keeping his hostility from coming out in breath that he fears might express rage. Unconsciously and childishly perhaps the adult asthmatic patient fears that if he shows his hostility, he will be thought "bad." He fantasies that he might act in a way that would impair his supply of love. Physiologically, the result is that he indeed impairs his supply of oxygen. His anger, instead of having been directed outward toward the person against whom he feels it, has been turned inward against his own person. By becoming sick, he has hurt himself.

To summarize, then, the physician can take for granted that in terms of the asthmatic patient's emotional disturbances, he is confronted with four major psychotherapeutic tasks.

1. To feed the patient's affect hunger.
2. To lessen the patient's fear of rejection.
3. To reduce the anxiety that makes the patient block the expression and even the awareness of the anger within him.
4. To help the patient release his anger so that it brings harm neither to others nor to himself.

Obviously the doctor cannot always respond at once to all these emotional needs of the patient. In fact, it may be dangerous to do so. Attention to emotional needs should be carried out in fairly well-defined sequence according to a regime which we will attempt to describe.

First in this regime attention must be placed on the feeding of the affect hunger and on lessening the fear of rejection. Only after this can the

doctor safely turn attention to helping the patient feel less anxious about unblocking and expressing his hostility.

How can the doctor take the first steps of feeding affect hunger and lessening the sense of rejection? He does this most effectively by accepting the role of a "good," dependable and trustworthy parent with which the patient invariably wishes to endow him.

Some physicians accept this role intuitively and variously in terms of their personalities, their attitudes and feelings and their dedication to the practice of medicine. However, they can plan more effectively to accomplish it when they add to it the conscious awareness of the psychodynamic function of what they do.

In order to see how such a role can be taken and furthered on a conscious basis, let us illustrate with an actual experience.

A woman of forty was seen for the first time in answer to an emergency call shortly before midnight. When the physician arrived, the resuscitation squad from the nearby fire department was busy with her. It was their fifth visit that night and a repetition of what had been going on for several nights. The patient, cyanotic and laboring for breath, was being supported by two of the squad while the third administered oxygen. They reported that each of their visits had brought her relief. But no sooner had they reached their station when they were called to return. Each time they had come with good grace and had promised to return as often as necessary.

In order to facilitate the patient's fastening on him the desired role of a good and acceptant parent, the physician consciously followed certain procedures.

The leisurely approach is one of these procedures since hurry can readily be taken as rejection. Unhurriedly, he examined the patient, and afterwards indicated that he had time to stay and hear more about her.

At this point, instead of keeping the husband in the room, he suggested that he wanted to talk with the patient alone. He thereby indicated to her that she was like a preferred child and that his primary concern was with bringing comfort to her rather than to others in the family. He also called her, as a parent would, by her given name. He gave her a chance to talk and he listened attentively.

She brought out that the previous physician had failed to return her call in answer to several frantic messages left for him. She had characteristically taken this in the sense of parental rejection. Her complaints were like the panicky cries of a deserted child. Nonetheless the doctor heeded them, respecting their importance to her.

That these measures were effective became quickly apparent. Although no medication had been given, her breathing eased.

The doctor had now established himself as a warmly interested parent. He must, as well, prove himself trustworthy.

He assured the patient, at the time of departure, that he would be avail-

able, no matter how often she called during the night. She tested him out by calling him three times between midnight and dawn. He paid a visit each time, although at none of these calls was her physical condition severe enough to necessitate seeing her.

The morning brought with it a problem that would need to be carefully handled. The doctor knew that he would be unavailable between eight a.m. and noon, except for short breaks at stated hours. Should the patient telephone and find him unexpectedly unavailable, it might throw her back into fantasied rejection and asthma. And so he told her clearly just what times she would be able to get through to him and explained that at other times he would be out of reach.

"I know you'll be worried," he said, "and perhaps a bit angry at me. But I believe you can manage all right."

Thus, early in the relationship, he put realistic limits on how much of demanding could be acted out with him. But at the same time he showed that he considered her feelings as real entities. He was not calling on her to cover them with a brave front. Nor was he calling on her to talk about her anxiety and her anger at too early a time. He was simply and in kindly fashion accepting her feelings as realities not to be belittled. By stating them himself he was laying a groundwork for her to bring them out more openly in the future when she would feel safer through having acquired a greater trust in him.

The following night she called twice and was visited each time. After this the visits dwindled to once daily for four days to reassure her of continued interest until she could come to the office for treatment.

During this time the only other medication consisted of mild sedation and the use of the nebulizer which she requested, although it was obvious from watching her use of it that little if any of the nebulized solution entered the bronchi. As she talked it became clear that she took such medication as a comfort which a parent allows a child.

Throughout a rather long initial period the major concern had to do with satisfying her hunger for affection and reassuring her that she was not rejected even though there had to be limits set on her demands.

When these goals had been achieved the doctor was ready to take the next steps. He was ready to help the patient further reduce her anxiety to the point where she would feel relatively safe in unblocking her anger.

How soon to permit a patient to recognize that he is angry is a delicate matter. In some patients, particularly in children, anger can be safely brought into the open more quickly. At all times, however, the doctor must keep his finger on the pulse of the patient's anxiety.

In this particular patient, the frank expression of anger came very slowly since it was blocked by intense anxiety. Although it insinuated itself now and again, as in the complaint about the former physician, she remained quite unaware of its presence. Then, one day during an acute attack, the doctor noticed some sharpness in her voice as she spoke

of her mother. In order to test her readiness to accept her own hostility, the doctor put her feelings into words. He said, "Your mother gets under your skin sometimes, doesn't she?"

Suddenly, despite the shortness of breath which caused her difficulty in speaking, she exploded, "She certainly does. Sometimes she's more of a hindrance than a help." Then, just as suddenly, she pulled in. "But I'm truly grateful to her. She's such a wonderful woman and she helps me so much."

By such neutralizing statements, the patient again and again gave evidence of her great anxiety. Other evidences came through evasion, going off on tangents, crying, appearing embarrassed, being taken by coughing and wheezing spells, denials and self-condemnation and by ever new physical complaints.

In order to reduce the anxiety and build greater tolerance for her own anger, the doctor once more consciously used his role of parent. In this role, he knew that anger at him would be inevitable and that his acceptance of it would be crucial.

He must concretely let her see that he could accept her hostility toward him. It was for this reason he had dropped the remark very early in his contact with her, "You'll perhaps be a bit angry at me," for not being able to reach him during the day.

For the same reason he remained watchful for further evidence of anger toward him, as for some imagined neglect or slight. When he observed such evidence, he himself remarked on it. He did this in such a manner as to communicate that her anger at him did not in any way interfere with his continuing interest and care.

Furthermore he made comments himself on situations that he knew must stand to her for insult or neglect. He said, for instance, "I suppose you were put out when you couldn't get me right away on the telephone last night. I don't blame you. It was hard." . . . He said, "I know you were angry at me for writing the prescription for only twenty-five sleeping tablets instead of the fifty you asked for. It made you feel as if I were papa or mother saying, 'No, you can't have what you want.' "

That this sort of technique did pave the way for unblocking and ventilation was evident one morning when she came to the office in an acute attack. She was late for her appointment, apologized profusely and gave as an excuse that her husband who drove her to the office was not up in time. The doctor knew that her husband always depended on her to be awakened. It was therefore obvious that her tardiness was something she herself had brought about.

"Maybe you didn't want to come in and see me," he remarked.

There was a momentary blaze of anger in her eye. But, quickly pulling herself together, she said, "Maybe you're right. I was kind of mad at you last time for keeping me waiting."

The doctor answered, "Yes, I know it was exasperating." Hereby he

both recognized and accepted her resentment. He did not try to evade the anger by making excuses for himself.

At this point her wheezing stopped.

Although as with most asthmatic patients she never became very voluble or intense in the expression of her anger, nonetheless with the continuance of this procedure she became able to bring out her resentments more freely not only toward the doctor but toward other people important in her life.

She was an only child of parents who had been greatly disappointed that they had had a girl instead of a boy. More or less obvious demands on the part of the parents that she satisfy their longing for a son led her to be a tomboy in an attempt to retain their love. With the onset of menstruation these defenses failed. She could no longer escape the fact of their rejection by acting out her fantasy of not being a girl. Neither did she dare express her frustration and fury at them for their nonacceptance of her. The repression of her anger was manifest in her asthma. Although, in the present, her parents showed their preference for a boy in blatantly preferring her husband to her, her resentment over this she also kept concealed.

One day, however, after she had been in treatment for four months she came into the office wheezing badly. The doctor asked her, "What's been happening?"

"Well," she said hesitantly, "my husband said this morning he thinks my mother and father wanted a boy very much. They said to him, so intensely, 'Now we have a son.' That makes me remember. They told me that before I was born they had a name picked for a boy. And yesterday my mother said to me, 'If anything goes wrong with your marriage (this was her second one) it'll certainly be your fault.'"

Believing now that she had courage enough to face and bring out her hidden anger, the doctor asked, "How did that make you feel?"

"I guess he was right, my husband. They didn't want me."

"And that couldn't help but make you angry."

"You're right," she nodded and tears rose to her eyes. "When my mother said that yesterday I guess I was mad. I feel mad at her now. To see this, somehow, makes me breathe easier." And her dyspnea stopped.

A similar sequence of events happens repeatedly in many instances. A patient comes into the office in varying degrees of respiratory distress. He gains relief after giving vent to anger, sometimes at the doctor, sometimes at parents, spouse or even at a child—in short, at whomever he fantasies as the unloving parent at the particular time.

When treatment stops short of helping the patient ventilate his hostility, there is more likelihood of recurrence of the acute attacks.

Nonetheless some patients never arrive at the stage where their anxiety

permits the safe ventilation of anger. No matter what the doctor does, the patient evades the direct expression of hostility. The doctor must then, along with his medical treatment, continue to rely on the emotional support which comes with his assuming the parental role.

All that has been said regarding the therapeutic approach toward the emotional components in the acute attacks of bronchial asthma is applicable as well in their prophylaxis.

Properly then the same procedures should be carried out whenever and wherever the doctor makes contact with the patient, in the office, home or hospital, whether in a prolonged consultation; in a telephone conversation or in the brief moment of giving an injection.

Emphasis should be placed here too on the role of office and hospital personnel who come in contact with the patient. In fantasy the patient is apt to see them as part of the doctor's family. He is apt to imagine them at times as rival siblings. As such they will come in for their share of demands and hostility from him, and therefore they should be prepared to take these without offense.

At times, too, the patient is apt to identify the secretary, nurse or technician as a parent of lesser importance and confides in her instead of in the doctor. This seems safer because the idea of losing a lesser parent's love is not so frightening. Such a move, however, destroys the therapeutic relationship between the doctor and patient. The patient, in order to justify what he has done, may too readily fantasy that the doctor has rejected him. And the doctor, unaware of what is happening, cannot take care of the fantasied rejection.

It is therefore of utmost importance when a patient begins to confide in an assistant that the assistant should say with all sincerity and kindness, "Better tell that to the doctor." This enables the doctor to keep the therapeutic relationship in hand.

CONCLUSION AND SUMMARY

In the foregoing, a regime for handling the acute attack of bronchial asthma has been outlined and described in terms of the psychodynamics of the asthmatic pattern. It consists essentially of approaching the attack of asthma by feeding the affect hunger, by lessening the fear of rejection, and when possible by lessening the patient's anxiety over his hostile components and helping him to release them.

A few concrete techniques have been described. These are not all-inclusive. They are merely suggestive of the type of procedure which each physician can explore according to what his personality dictates and what he himself feels he can carry out.

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LOCUST SENSITIVITY

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INSECT sensitivity causing skin irritation, allergic rhinitis and asthma sometimes with an environmental[6] and seasonal incidence has been described as occurring in various parts of the world. Severe constitutional allergic reactions or even death may occur in a sensitive patient when stung by a bee or wasp. The symptoms produced in the allergic patient depend on the degree of sensitivity and also the manner of introduction of the allergen into the body.

Symptoms of insect inhalant sensitivity are not so dramatic and the cause may not be so obvious to the patient.[2,3,11] The whole subject of insect sensitivity was well reviewed by Brown[1] in 1944. There seems to be no account in the English language of locusts causing allergic symptoms though a report of locusts causing asthma has been described from Spain.[5] Although no confirmatory skin tests were performed in this instance, there seems to be no doubt from the observations of the patient that his seasonal asthma only occurred when locust swarms were present.

MATERIAL AND METHOD

My interest in locust sensitivity dates from 1948 when I was assured by a patient who was receiving treatment for a seasonal hay fever that he was also sensitive to locusts. He was working at an experimental research station (A) breeding locusts. He stated he had a mild perennial allergic rhinitis when handling the insects. The patient was transferred from the locust laboratory to a new locality. Since this time his seasonal hay fever has been well controlled by preseasonal injection therapy with grass pollen extract and his perennial symptoms do not now occur. The possibility of locust sensitivity was investigated and anyone coming in contact with locusts was tested with locust extracts. The locusts used were adult *Locusta migratoria* of average weight about 1 gram and *Schistocerca gregaria,* 2 grams in weight. Fifty male and female locusts were killed with chloroform after keeping on ice overnight. They were then macerated with pestle and mortar and defatted with acetone. The acetone was filtered off and the dried residue weighed and extracted with buffered saline to give a 1:10 dilution (wt./vol.). Extraction was allowed to continue for forty-eight hours with occasional stirring before gross filtration and finally Seitz filtration was carried out. The extract had a protein nitrogen content of 0.38 mg/ml.

An analysis of the results is shown in Table I. It is apparent that among

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TABLE I. ANALYSIS OF CASES (AT CENTRE A) IN CONTACT WITH LOCUSTS

Patient	Age	Sex	Family History	History of Locust Contact		Results of Skin Tests			Symptoms from Locusts	Other Allergies
				Years	Nature of Exposure	Grass Pollen	Locust Male	Locust Female		
H.H.	36	M	+	3	Light	−	−	−	No	
J.C.	21	M	−	4	Heavy	−	+	+	No	
C.S.	36	M	+	1	Light	−	−	−	No	
F.H.	27	M	−	2	Heavy	−	++	+	No	Summer urticaria
J.N.	34	M	−	3	Light	−	−	+	No	
B.R.	20	M	+	1	Heavy	−	−	−	No	
J.W.	25	M	+	2	Moderate	+++	+	++	No	Summer hay fever
J.T.	19	M	−	1	Light	−	−	−	No	
D.D.	33	M	−	2	Light	+++	++	++	No	Summer hay fever
G.S.	33	M	−	17	Heavy	++++	++	++	No	Summer hay fever Urticaria 6 months
W.S.	31	M	+	3	Moderate	−	++	++	Yes	
G.B.	17	M	−	1	Moderate	+++	+	++	Yes	Summer hay fever
S.P.	23	F		1	Light	+++	+	+	No	Summer hay fever
E.G.	30	M	−	2	Moderate	−	−	−	No	
J.M.	26	F	−	2	Heavy	−	−	−	No	
F.B.	43	M	−	1	Light	−	−	−	No	Rhinorrhoea
V.W.	18	F	+	1	V. light	++++	−	−	No	Summer hay fever
R.O.	28	M	−	10	Light	+++	++	++	No	Summer hay fever

TABLE II. RESULTS OF SKIN TESTS WITH LOCUST EXTRACTS IN PATIENTS WITH SEASONAL HAY FEVER, I.E., PATIENTS WITH NO KNOWN CONTACT WITH LOCUSTS

Size of Skin Response Indicated by number of sign	Number of People Giving the Response When Tested with	
	Locust Faeces	Locust Bodies
++	2	2
+	7	5
−	62	64

the eighteen workers tested there is a high incidence of allergic complaints as seven of them had a definite summer hay fever and two more had symptoms which were probably allergic. Two of the patients described definite symptoms from locusts. The symptoms of a perennial allergic rhinitis when in contact with locusts has already been described as the first case seen. The other patient, whose brother had seasonal hay fever, stated that only locusts caused allergic symptoms. He had a localized irritation of hands and arms when handling locusts and asthma when cleaning out their cages. This he did on occasional weekends when his duty term came round. Interestingly he had complained for the past year that only on his duty weekends did he have a chesty cold with a wheeze.

It will be noted from Table I that confirmatory positive skin tests were obtained in the patients with symptoms from locusts. Five other patients also gave definite positive skin tests (++) to locusts which were presumably of sub-clinical importance as they complained of no symptoms. Only V.W. of the allergic patients who had a marked seasonal hay fever, did not give a positive skin reaction to the locusts, but her contact had been very slight indeed for one year.

The possibility that nonspecific skin reactions were being obtained from

the testing material was investigated as follows: Seasonal cases of hay fever giving marked positive skin tests to grass pollen extracts were tested with locust extracts. The results show that in seventy-one seasonal

TABLE III. THE NUMBER OF POSITIVE AND NEGATIVE SKIN RESPONSES IN ASTHMATIC PATIENTS USING THE COMMON ALLERGENS COMPARED WITH THE INCIDENCE WHEN TESTING WITH LOCUST AND COCKROACH EXTRACTS

Using Common Allergens whether positive or negative skin responses	Number Tested	Locusts		Cockroach	
		Positive	Negative	Positive	Negative
Positive	27	7	20	4	23
Negative	27	0	27	0	27

TABLE IV. RESULTS OF POSITIVE AND NEGATIVE SKIN TESTS WITH LOCUST AND COCKROACH EXTRACTS IN 91 HAY FEVER PATIENTS, I.E., PATIENTS WITH NO KNOWN CONTACT WITH LOCUSTS

Number Tested	Locusts		Cockroach	
	Positive	Negative	Positive	Negative
91	12	79	9	82

hay fever cases tested in 1951, two cases gave a definite positive response (++), seven gave doubtful positive responses (+) and sixty-two were entirely negative to locust extracts. This is shown in more detail in Table II. The test material used was an extract of a mixture of male and female locusts and their faeces. The faeces were found to be a particularly potent source of trouble to locust sensitive patients.

INVESTIGATION OF POSSIBLE COCKROACH SENSITIVITY

As two out of seventy-one patients who had never been in contact with locusts gave a definite (++) skin response to a locust extract, tests were carried out with extracts of the entomologically allied cockroach. The patients tested were intrinsic and extrinsic[7] asthmatic and seasonal hay fever patients. The results are set out in Table III and IV. Fifty-four consecutive asthmatic patients were tested with common allergens. Twenty-seven gave positive skin responses and an equal number negative skin responses. All the patients giving a negative skin test to the common allergens also gave negative skin test to cockroach and locust extracts. Of the twenty-seven positive reactors, seven reacted to locusts and four to cockroach. (Table III). No patient in this series reacted to cockroach who did not react to locust. These findings suggest that there is an antigenic similarity between locusts and cockroaches.

TABLE V. ANALYSIS OF CASES (AT CENTRE B) IN CONTACT WITH LOCUSTS

Patient	Age	Sex	Family History	History of Locust Contact		Results of Skin Tests			Symptoms from Locusts	Other Allergies
				Years	Nature of Exposure	Grass Pollen	Locust Male	Locust Female		
P.D.	26	F	+	1½	Heavy	−	+	+	No	
A.T.	28	F	−	2½	Moderate	−	−	−	No	Urticaria 3 yrs.
G.S.	37	M	−	9/12	Light	−	−	−	No	
D.G.	42	M	−	6/12	Light	−	−	−	No	
J.B.	21	M	−	4/12	Light	+	+	+	No	
G.H.	28	M	+	1	Light	−	++	++	No	Rabbits cause rhinorrhoea
V.D.	47	M	−	28	Light	−	−	−	No	Spring hay fever
J.C.	24	M	−	8/12	Moderate	−	++	++	No	
M.R.	40	F	−	5	Light	−	−	−	No	
A.B.	22	F	+	1/12	Heavy	+	−	−	? yes	Slight Summer hay fever
P.M.	19	F	−	4/12	Heavy	−	−	−	No	
P.E.	27	F	+	4½	Heavy	−	+	+	Yes	
R.C.	21	M	+	4/12	Heavy	−	−	−	No	
K.G.	28	M	−	8	Moderate	+	−	−	No	
J.M.	20	F	+	2½	Moderate	−	++	++	No	
H.J.	25	M	+	4½	Heavy	+++	+++	+++	Yes	Summer hay fever

OTHER LABORATORY WORKERS WITH LOCUST SENSITIVITY

In 1951 a further opportunity to study other cases of locust sensitivity arose at a different research institution (B), where in one room over a third of a million locusts a year were hatched for experimental purposes. The results of investigations on the sixteen persons working in the laboratory are set out in Table V. In contrast to the previous laboratory staff, there was a much lower incidence of known allergic complaints. Yet there was more intimate and heavy contact with larger numbers of locusts, though for some of the staff the contact although heavy had been of short duration. It was noted that the daily cleaning out of the dry debris which collected at the bottom of the cages, particularly upset patients sensitive to locusts. This debris becomes powder dry because each cage is heated by an electric bulb. The debris itself is largely locust faeces of constant size.

Two patients of the sixteen cases examined had definite symptoms of asthma from locusts. After working for two years with locusts "P.E." found that her skin became very irritable when locusts nipped it. She also noticed a wheeze would develop when working with locusts. She had a marked family history of asthma. Skin tests showed small positive responses to four different locust extracts used but she gave no other positive not even to cockroach. It would seem her only sensitivity was to the locust antigen. The history of "H.J." and his progress are worth reporting in more detail.

Case 1.—H.J., a man aged twenty-five years, had worked for four and a half years with almost daily heavy contact with locusts. A maternal aunt had a summer hay fever. He noticed a mild catarrh and sneezing in the summer of 1948. This did not worry him but in the autumn of 1949 after three years' contact with locusts he remembers he sneezed and had rhinorrhoea when in the locust laboratory. His hay fever in the summer of 1951 seems to have been bad enough for him to go to

the doctor for advice. He had a wheezy cough in May and finally he realized that his complaint was asthma due to locusts, as it always began within minutes of entering the laboratory. His asthma continued throughout the winter and he only lost the complaint on taking a fortnight's holiday. He had been told that his complaint was due to the state of his nerves and general overwork. I first saw him on January 10, 1952, when skin tests confirmed his sensitivities. There were positive responses to the grass pollens, to three different locust extracts, and the largest skin response of all was to locust faeces. He did not react to cockroach or fly. A desensitizing course of injections was started using the locust faeces as the antigen. Injections were given every other day or so beginning with 40 Noon units and finishing with 100,000 units, the course being one of twenty-five doses. He was very delighted with the result of the treatment. If he dealt with locust en masse he wore a mask in case he developed asthma but normally he took no precautions and had no trouble. He took continuation doses of 50,000 units once a month but found that after the third maintenance dose he developed asthma. This was prevented by reducing the dose to 25,000 units a month and by taking a suitable antihistaminic (Ambodryl) when he received the injection. Later the time between maintenance doses was shortened to three weeks as he noticed a return of locust sensitivity during the last week. After nine maintenance doses of 25,000 units the dose was again reduced to 15,000 units. He now describes his present state as "for all intents and purposes 'cured' though the face mask is still necessary in high concentrations of locusts." The size of his skin test to the pollens remains unchanged, while that to locust is reduced to one-quarter of that before treatment. He states that he has found that pricking his skin with one of the tarsal spines from a locust will cause a local irritating wheal and flare. Prausnitz-Kustner tests could be performed satisfactorily with his serum.

The workers at this last laboratory were reviewed after six months. It was thought that further cases of sensitivity to locust might be found by repeating the skin tests, particularly on those with a continuous contact. "J.M." is a case in point, although shown as having no symptoms from locusts, she had marked positive skin tests and on close questioning it was found that she had been off work twice for short periods with "bronchitis." She also stated she had had catarrh but that this disappeared when on holiday.

"A.B." has a more definite history. She also is shown as having no symptoms from locusts but she had only worked for four weeks with locusts when first seen. She had a marked family history of allergic disorders, she herself had a very mild sensitivity to grass pollen and when first seen gave a positive response to only one (faeces) of the four locust skin testing extracts. Six months later using the identical extracts all were positive—though not markedly so. She now stated that she had a persisting "cold" since working with locusts and that they caused her to sneeze. Her fellow worker whose skin tests remained negative stated, however, that she too developed catarrh and frequent "colds."

It seemed likely that further patients with locust sensitivity could be found at laboratories using the insects experimentally. One comes from Scotland where a research worker found that locusts were causing her asthma.

Case 2.—Miss P. C., aged twenty-eight, had a family history of the allergic disorders, and began to have a summer hay fever at the age of fifteen years. During the last four years she has noticed few symptoms from grass pollen. She began working with locusts in 1948. The contact with them was close and heavy as her time was largely spent dissecting them. Four months after beginning this work she developed "sinusitis." Proof puncture produced no pus and eventually she was told her trouble was "allergic" in type. A year after starting work with locusts, she had developed a wheezing cough and six months later in March when the condition was worse the diagnosis of asthma was made. The asthma slowly became worse during the next twelve months. She then found that her asthma dramatically disappeared when doing some writing away from locusts. On returning to locust work for one day asthma developed on three separate occasions. I first saw her on December 23, 1952, when she was on holiday in London and apparently well. Skin tests showed positive responses to all grass pollens tested, to mixed household dust, to hen feathers (she stated pigeon feathers upset her) and horse scurf. She gave positive responses by skin test (prick method) to all locust extracts tested. Locust faeces and a mixed locust extract gave ++ positive response, but the female and male *Locusta migratoria* gave a ++++ positive response with large pseudopodia. This was interesting as she has only worked with *Locusta migratoria* but this was unknown to us when performing the skin tests. Interestingly she gave a negative skin response to cockroach and fly. Other skin tests against pollens other than the grasses and various animal scurfs and moulds were all negative. The patient has been started on a desensitizing course using increasing strengths of *Locusta migratoria* extract.

Another patient lives in Copenhagen. A man, aged thirty-five, after working with locusts for two months found that they caused an urticarial rash on the hands, sneezing and a bronchitis which was finally labeled as asthma. Information has also been received of a female research worker and expert on locusts in the United States who develops asthma on coming in contact with them. (Dr. Uvarov, personal communication).

DISCUSSION

Various interesting possibilities arise as a result of this investigation. It has been seen that there are some grounds for believing that there is a cross antigenicity between locusts and cockroaches. Locust sensitivity is unlikely to occur in this country except in laboratories where they are used. It was interesting that locust faeces were the most potent cause of allergic symptoms in one of the sensitized patients. Cockroaches are, however, not uncommon in many houses and institutions. When food supplies are plentiful cockroaches can leave about a considerable amount of faecal matter. When dry it becomes incorporated into the dust. Here then is another possible component of household dust that specifically could upset a sensitized patient. This aspect of household dust sensitivity does not seem to have been considered except by Sutherland[9] who pointed out that dust antigens among other things consist of scales, bacteria and insect *faeces*.

Investigating locust sensitivity might help to elucidate the problem of the role of the exogenous factor in the development of allergic com-

plaints. Are those who develop a sensitivity to locusts those who have an "allergic disposition?" By this is meant (1) those who already have a known allergic complaint due to a known sensitivity, (2) those who have

TABLE VI. ANALYSIS OF ALLERGIC AND NON-ALLERGIC SUBJECTS IN CONTACT WITH LOCUSTS

Type of Patient	Number	Positive Skin Test to Locust	Locust Sensitive
Normal non-allergic (no family history)	12	4	0
Normal with positive family history	8	4	1
Normal but positive skin tests to some common allergens	2	1	0
Known allergic patients	12	9	3
Total	34	18	4

no allergic complaint but have a family history of the allergic disorders, and (3) those who do not come under either of the above headings, but who during routine skin testing gave positive results and had thus circulating non-precipating antibodies to common allergens. The latter can be considered to have a sub-clinical or latent allergy. Table VI would suggest that exposure to locusts in known allergic patients, is more liable to cause specific allergic symptoms than in so-called normal individuals.

In this series of thirty-four people under investigation it would appear that the normal person is unlikely to develop symptoms. Even so, some of these (four), as they gave positive skin tests, should be transferred from the normal group to the allergic prone group. One patient whose allergic proneness was a positive family history has become sensitized, while of the twelve with active allergy present, three only have not developed positive skin tests to locusts and three others are acutely conscious of allergic complaints when in the presence of the insects.

Our follow-up period has not been long enough to decide whether allergic predisposition influences the time taken for symptoms to develop. This problem has been carefully considered by Schwartz.[8] After studying fifty probands with bakers asthma, he came to the conclusion that the complaint was "due to an inherited predisposition to asthma in general." The period of sensitization must depend upon many factors, for one and the same allergen may sensitize in a few months or may take twenty-five years or longer. One extremely important factor which is most difficult to measure satisfactorily is the *quantitative* aspect. This may affect not only the degree of sensitivity as shown by clinical symptoms, but also the time taken for sub-clinical symptoms to become manifest. This aspect of the quantitative importance is well shown in pollen sensitive individuals by the last two botanists employed in our Allergy Department. Neither had previous symptoms of hay fever before starting pollen collection though both were found to have positive skin tests to various pollens. Both

these botanists developed hay fever and an associated asthma within a few weeks of starting work in the pollen production room where there is always an extremely high concentration of pollen in the air during collecting time. This quantitative aspect is very important in locust sensitivity as shown by the results of skin testing and clinical sensitivity. A heavy contact with locusts occurring when the patient has active sensitivities present—in the cases under review a patient with summer hay fever—eventually produced clinical symptoms in all these locust workers. Is it possible to become sensitive to locusts if not an allergic prone individual? "P.E." who has had constant heavy contact with locusts for four years now develops asthma when working with them. Apparently she has no other sensitivity by skin testing or from her history, but she has a marked family history of allergic diseases (her grandmother, mother, brother and a maternal cousin all have asthma), so she too could not be considered normal but comes into the allergic prone group.

Since interest in locust sensitivity began, it has been possible in some cases to follow the start of locust sensitivity as shown by skin tests previously negative becoming positive. Such patients with a latent allergy should be advised that allergic symptoms are likely to develop sooner or later if their work brings them into constant heavy concentrations of the allergen.

The antigenic components of the locusts, eggs to adults, and faeces are being investigated chemically in relation to skin sensitizing power. This work will be reported at a later date. Meanwhile it is hoped that with this report on locust sensitivity other reports will be forthcoming, particularly from persons coming in contact with locust swarms in the field.

SUMMARY

1. Various forms of insect sensitivity have been described previously but locust sensitivity has never been investigated.

2. It was found that some laboratory workers using two different kinds of locusts, *Locusta migratoria* and *Schistocerca gregaria*, developed an irritation of the skin, allergic rhinitis and asthma from close contact with the insects.

3. Of thirty-four workers coming in contact with locusts, four had symptoms of allergic rhinitis and asthma from them when first examined. Fourteen others had a sub-clinical sensitivity as shown by positive skin tests.

4. There seems to be some antigenic similarity between locusts and cockroaches as four out of seven patients reacting by skin tests to locust extracts reacted also to cockroach.

5. Clinically and by skin tests locust faeces caused inhalant allergic symptoms and an extract of locust faeces was successfully used in one of the patients for hyposensitization.

6. Exposure to locusts in known allergic patients or patients who have an allergic disposition, is more likely to cause specific allergic symptoms than in so-called normal individuals.

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REFERENCES

1. Brown, E. A.: Progress in Allergy. Insects and allergy. Ann. Allergy, 2:235, 1944.
2. Figley, K. D.: Mayfly (Ephemerida) hypersensitivity. J. Allergy, 11:376, 1940.
3. Gaillard, G. E.: The Aphid—an insect allergen. J. Allergy, 21:386, 1950.
4. Jamieson, H. C.: The house fly as a cause of allergy. J. Allergy, 9:273, 1938.
5. Ludmer, N.: Asma provocado por la langosta. Semana med., 1025, 1935.
6. Ordman, D.: Sewage filter flies (Psychoda) as a cause of bronchial asthma. South African M. J., 32 (Jan.) 1946.
7. Rackeman, F. M.: A working classification of asthma. Am. J. Med., 3:601, 1947.
8. Schwartz, M.: Heredity in bronchial asthma. Acta Allerg., 5, Supplementum II, 1952.
9. Sutherland, C.: The allergen of house dust. M. J. Australia, 1:583, 1945.
10. Urbach, E., and Gottlieb, P. M.: Asthma from insect emanations. J. Allergy, 12:485, 1941.
11. Wittich, F. W.: The nature of various mill dust allergens. J. Lancet, 60:418, 1940.

III SPANISH CONGRESS OF ALLERGY

The Third Spanish Congress of Allergy will be held January 6-13, 1954, at Las Palmas, Santa Cruz de Tenerife, Canary Islands. The scientific program includes the following:

1. Radiology of Asthma by Drs. Manchon and Foouchtman of Barcelona, and Lara Roldan and Alberto Acceituno of Madrid.
2. Pollinosis by Dr. Alemany Vall.
3. Infectious Asthma by Professor Jimenez Diaz and Drs. Laoz and Ortego Nunez.

An extraordinary technical study on "Serodiagnostico y especialidad de las pruebas en alergia" (Diagnosis by the use of Serum and Singularity of the tests in allergy) under the direction of Drs. Perianes, Segovia Arana and Aguirre Jaca.

For further information, write to the Secretaria del Comite Organizador, Dr. A. Capote in Santa Cruz de Tenerife, Rambla General Franco 84.

SENSITIVITY REACTIONS TO PENICILLIN IN CHILDREN

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SINCE the therapeutic use of penicillin has become widespread, an increasing number of sensitivity reactions are being reported, many of which are serious enough to cause grave concern to physicians and the public. Many of these reactions are referred to in reviews by Brown[1] and by Smith and Walker.[22] The incidence of reactions, as reported by various authors[4,11,12,25] varies from 2-10 per cent. The types of sensitivity reactions vary from mild skin rashes, which do not necessitate discontinuing the drug, to severe anaphylactic reactions which are sometimes fatal. Practically every kind of skin eruption has been attributed to penicillin hypersensitivity and many other types of reactions have been recorded in the literature. (Table I). According to Feinberg[4] the most common reaction is the delayed "serum sickness" reaction occurring several days after administration of the drug and commonly accompanied by urticaria, angioneurotic edema, arthralgia, swelling of the joints and fever. The incubation period is usually ten days but may be only four to five days or as long as three weeks. The duration of the illness is commonly one to two weeks but the urticaria and angioneurotic edema may continue longer in some patients. Friedlaender and Friedlaender[6] also believe that urticaria is the commonest reaction. It may occur shortly after the administration of penicillin is begun, during the course of therapy, or at some period after treatment is concluded. The reaction may be minimal and disappear even while penicillin is continued or it may be extremely severe and progress to serum sickness. These authors have encountered cases of chronic urticaria of several years' duration which were initiated by a "serum-sickness type" reaction following the use of penicillin.

Of the sensitivity reactions to penicillin, the most serious is anaphylactic shock. Such reactions are becoming more numerous in the literature and are frequently being reported verbally without being published. Many of these are non-fatal but we have been able to find fourteen fatal anaphylactic reactions recorded in the literature. From verbal reports, however, it is quite apparent that this is not a true picture. For example, an editorial in the *Journal of Allergy*[3] refers to four fatal anaphylactic reactions which up to that time had not been reported. We know of two more in Toronto which have been reported in the newspapers but which we have not permission to report in detail in the medical literature. The fourteen reported cases plus the two Toronto cases are summarized in Table II.

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Presented, in part, at the Annual Meeting of the Canadian Paediatric Society, June, 1953.

TABLE I. SENSITIVITY REACTIONS REPORTED DUE TO PENICILLIN

Organs Involved	Types of Reaction
Skin	Dermatitis Urticaria—immediate or delayed Angioneurotic edema Bullous dermatitis Erythematovesicular eruption Vesicular eruption Purpura (thrombopenic and non-thrombopenic) Papular erythema Exfoliative dermatitis Papulo-pustular eruption Contact dermatitis Fixed drug eruptions Scaly erythematous reactions Scarlatiniform eruption Morbilliform eruption Erythema—multiforme like eruptions Pruritus Dermatophytosis-like reactions Flaring of existing dermatoses Miliaria Erythema nodosum Eczematoid dermatitis Atopic dermatitis Dermatographism Local Arthus phenomena Local thrombophlebitis Local inflammation Local abscesses
Mouth	Sore mouth Hairy tongue Thrush Perleche Vesicular cheilitis
Lung	Asthma Loeffler's syndrome
Nose	Vasomotor rhinitis
Eyes	Conjunctivitis Blepharitis
General	Serum-Sickness-like reaction Collagen disease Polyarteritis Drug fever Convulsions and encephalitic symptoms Photosensitivity Hematuria Anaphylactic shock (fatal and non-fatal) Any phenomenon occurring in hypersensitivity Renal dysfunction with albuminuria and cylinduria Edema of face, lips, pharynx, larynx, and pulmonary mucosa Periarteritis nodosa

Friedlaender and Friedlaender[6] point out that many of the reactions in the early days of penicillin therapy were undoubtedly related to impurities, and that many individuals who reacted violently to earlier preparations, can tolerate present commercial aqueous suspensions without untoward effect. Keefer[17] states that the incidence of reactions is twice as high in those patients who are allergic to other things. Levin and Moss[13] report that sensitization to penicillin is rare in children and allergic children are no more liable to sensitization than are non-allergic children. They also note that in approximately 1,000 injections given to 226 allergic children, no important local or general sensitization reactions were observed other than a transient pruritic eruption in one patient.

All of the reported reactions need not be due to penicillin itself as pointed out by Reyer[18] who classifies penicillin dermal reactions as follows:

TABLE II. ANAPHYLACTIC DEATHS DUE TO PENICILLIN

Age of Patient and Occupation	Reaction and Mode of Administration	Previous Penicillin	Previous Reactions to Penicillin	Skin Tests Performed On or Before Fatal Injection	Allergy	Autopsy Findings	Author
1. Middle-aged man	30,000 u of penicillin q4h for 720,000 u. Vomiting, scarlatiniform rash, followed by rash increasing in severity and involving thorax, neck, face and arms. Despite discontinuation of penicillin, patient died 7 days after therapy instituted.	Amounts and type not reported.	Vomiting and rash previously after treatment by family physician with penicillin.	Not reported	None reported	Not reported	Wilensky[25], 1946
2. Thirty-nine-year-old woman	50,000 u (I.M.) penicillin followed in 5 seconds by a strange taste in her mouth and tongue with swelling in her nose and throat. Patient collapsed, became cyanotic and died immediately.	Three previous courses: (a) I.M. penicillin q3h for 7 days in 1947. (b) 4 daily doses of 300,000 u of procaine penicillin in 1948. (c) 400,000 u given as 50,000 u q3h in 1948.	None reported	Not reported	Severe bronchial asthma of 2 years duration and a previous 18 yr. history of grass hay fever.	Not reported	Waldbott[24], 1949
3. Fifty-seven-year-old labourer	I.M. procaine penicillin G. 300,000 u given and within 1½ minutes patient became cyanotic, coughed, had tonic muscular spasm and within another 30 seconds had gasping respirations, extreme cyanosis, unobtainable blood pressure and pulse weak and thready. Patient died 10 minutes after injection.	Oct. 1949 Previous procaine penicillin for lacerations and fractures.	Not reported	Not reported	Not reported	Autopsy revealed only increased mucus in the tracheo-bronchial tree.	Higgins and Rothchild[9], 1952
4. Not reported	Patient died within 5 minutes of receiving aqueous procaine penicillin.	Not reported	Not reported	Not reported	Bronchial asthma	Distended lungs with dilation of alveoli	Curphey[2], 1952
5. Not reported	Patient died within 10 minutes following an injection of penicillin and streptomycin.	Not reported	Not reported	Not reported	Not reported	Extensive mucoid exudate in smaller bronchi and alveoli.	Curphey[2], 1952
6. Twenty-two-year-old woman	Patient died 2-3 hours following injection of penicillin.	Not reported	None known	No	None known	Not available	Unpublished (Toronto)

7. Thirty-seven-year-old man	Patient died 1-2 minutes after s.c. injection of 1/10 cc of aq. penicillin strength unknown.	Amounts unknown	Previous urticarial reactions to penicillin.	No	None known	Not available	Unpublished (Toronto)
8. Forty-seven-year-old white man	In January, 1952, patient given 300,000 u of aqueous procaine penicillin I.M., immediately complained of a peculiar feeling in his chest similar to that experienced when he took troche previously. In a few moments patient collapsed into coma and died.	Following 1943 patient had 3 courses of penicillin of 2½ million, 5 million, and 7 million units with no ill effects.	In Nov. 1951, patient voluntarily took 1 troche of penicillin&fainted immediately but recovered spontaneously.	Not reported	Not reported	Not reported	Mayer[14], et al 1953
9. Sixty-seven-year-old man	On Dec. 5, 1951, 10 minutes after physical examination patient received 300,000 u of crystalline penicillin G while resting in bed. He felt nausea in a few minutes, vomited, became cyanotic, his lips, tongue became swollen and he died within 10-15 minutes.	300,000 u I.M. presumably of crystalline penicillin G in Nov. 1950. Dose repeated monthly until May 4, 1951 when it was recorded for the first time that procaine penicillin was given. This was continued monthly until July 20, 1951.	On Aug. 24, 1950 300,000 u of procaine penicillin were administered I.M. Immediately the patient collapsed, became unconscious and cyanotic, and was covered with a fine perspiration.	No	None reported	Respiratory system showed several small petechial hemorrhages beneath visceral pleura. There was evidence of chronic bronchitis and marginal emphysema. There was basiliar congestion of the lungs.	Thomson[23], 1952
10. Three and one-half-year-old child	Approximately one hour following an I.M. injection of procaine penicillin, the child lost consciousness and became dyspneic and died 2½ hours later.	I.M. injection of procaine penicillin day previous to fatal injection.	None reported	None reported	No history of previous asthma or other allergy.	A very few petechial hemorrhages on the surface of the lungs and brain and gross pulmonary emphysema.	Harpman[6], 1952
11. Sixty-seven-year-old woman	30 seconds following an I.M. injection of 300,000 u of aqueous procaine penicillin into the buttocks, patient complained of a strange taste in the mouth, tightness in the chest, and inability to breathe. Patient died before epinephrine could be given.	Repeated penicillin injections	None reported	Not reported	Bronchial asthma with chronic sinus disease. Allergy to aspirin.		Siegal[20], et al 1953

TABLE II. ANAPHYLACTIC DEATHS DUE TO PENICILLIN—CONTINUED

Age of Patient and Occupation	Reaction and Mode of Administration	Previous Penicillin	Previous Reactions to Penicillin	Skin Tests Performed On or Before Fatal Injection	Allergy	Autopsy Findings	Author
12. Fifty-four-year-old white man	15 seconds following an injection of 800,000 u of penicillin by family physician, patient experienced difficulty in breathing, cyanosis, and collapse. Patient died in two or three minutes.	Some 20 injections of penicillin previously without untoward result. Last dose prior to anaphylactic injection given 2 years previously.	None known	Not reported	Asthma for 10 years	Gross and microscopic findings showed emphysema, congestion of all the pulmonary vessels.	Feinberg[5], et al 1953
13. Forty-eight-year-old negro sailor	Immediately following 300,000 u of intramuscular penicillin, patient developed generalized pruritis, followed by nausea, vomiting, collapse (B.P. 60/40 mm Hg) convulsions, pulmonary edema, and rales in the chest. Patient died 5½ hours following injection.	Penicillin ophthalmic ointment had been used 5 mo. previously with no known reaction. Also previous oral penicillin.	Previous oral penicillin resulted in vomiting and pruritus.	No	Not reported	Lungs were dark purplish-red, non-crepitating, and edematous, and there was congestive hyperemia and atelectasis.	Feinberg[5], et al 1953
14. Twenty-seven-year-old negro soldier	10 minutes following an intragluteal injection of procaine penicillin in peanut oil with aluminum monostearate, patient vomited, became dyspneic, complained of dizziness and collapsed. This was followed by tonic convulsions, unconsciousness, cyanosis, and he was pronounced dead 20 minutes after injection.	No history of previous penicillin therapy.	None known	No	No history of previous allergy.	Cyanosis of the lips, puffiness of the eyes and face, mucus in the tracheobronchial tree, acute congestion of the lungs, and no sign of embolism.	Feinberg[5], et al 1953
15. Twenty-eight-year-old white soldier	Following I.V. penicillin 100,000 u in 1,000 cc of glucose and saline, patient developed a cold sweat, cyanosis, weak pulse, and a B.P. of 60/20 mm Hg. He died 2½ hours after symptoms first observed.	No history of previous penicillin therapy.	None known	No	No history of previous allergy.	Lungs were emphysematous and showed slight edema fluid: there was engorgement and congestion of blood vessels.	Feinberg[5], et al 1953

TABLE II. ANAPHYLACTIC DEATHS DUE TO PENICILLIN—CONCLUDED

Age of Patient and Occupation	Reaction and Mode of Administration	Previous Penicillin	Previous Reactions to Penicillin	Skin Tests Performed On or Before Fatal Injection	Allergy	Autopsy Findings	Author
16. Twenty-three-year-old white nurse	2 minutes following a self-administered injection of 200,000 u of crystalline sodium penicillin G, patient complained of shortness of breath, and shortly slumped down. Some 1½ hours later she was cyanotic with 6-8 respirations per minute and inaudible heart beat. She was dead 2 hours after injection.	Oral penicillin had been administered 8 months previously.	None known	No	None reported	A pink, frothy fluid was found in the bronchi and bronchioles. The subcutaneous tissue lateral to the upper third of the trachea was moderately edematous. The lower pulmonary lobes showed congestion and punctate hemorrhages, and the alveoli were edematous.	Feinberg[5], et al 1953

1. Epidermal contact—localized dermatitis in handlers such as nurses and physicians.
2. Dermal reactions—regardless of mode of application.
   (a) Reaction to penicillin.
   (b) Reactions to the vehicle, the base, or the culture medium upon which the penicillin was grown.
   (c) Non-specific reaction to the common mold antigen.
   (r) Herxheimer reaction from liberation of toxin from organisms killed by penicillin.
   (e) Reactions due to disturbance of symbiotic balance of organisms growing on the skin surface.

However, since all these reactions accompany the therapeutic administration of penicillin, they must all be considered in a discussion of penicillin hypersensitivity.

It has been observed that hypersensitivity reactions frequently occur in patients who have not had any known contact with penicillin previously. Goltman,[7] in a discussion of this, points out several possible mechanisms to explain this observation.

1. Transfer of sensitization *in utero*—Penicillin traverses the placental barrier and may be found in a ratio of ⅔ concentration of the maternal circulation in the fetal bloodstream.
2. Antigen-antibody reaction—will account for only a small percentage of the whole.
3. Hapten formation—Penicillin may act as a hapten in combination with serum protein as a sensitizing agent.
4. Common antigen effect—Trichophyton and perhaps other pathogenic fungi have antigens in common with penicillin.
5. Inhalant antigen effect, i.e., the inhalation of spores and mycelia of penicillium mold may presensitize the individual before any therapy with medicinal penicillin derived from the present source occurs.
6. Ingestant presensitization—Penicillium molds may be ingested and sensitize the individual in the form of food allergy.
7. Penicilliosis—Perhaps the presence of the mold in pathogenic form in a lung abscess may predispose to sensitization to penicillin administration. The presence of this organism in the bowel as a saphrophyte may well predispose to reaction in a similar manner.

While all of these mechanisms are theoretically possible, there is no proof that they are all in operation. Feinberg,[4] for example, states that there is no reason to believe that those persons who have respiratory allergy from airborne mold spores would experience acute systemic reactions from penicillin since he has shown that some penicillium sensitive patients fail to give a positive skin test to penicillin. Friedlaender and

Friedlaender,[6] likewise, have found that there is no immunologic relationship between penicillin and penicillium antigen, and that repeated administration of penicillin to fungus-sensitive individuals has been well tolerated. However, Peck and Hewitt[16] showed that common pathogenic fungi, which are responsible for many cases of dermatomycosis, are capable of producing an antibiotic substance which has similar properties to penicillin.

The development of sensitivity to penicillin may be expected to be influenced by the route of administration of the drug, whether intramuscularly, orally or topically. Hopkins and Lawrence[10] report penicillin to be a more frequent sensitizer of the skin than sulfonamides on local application. It is known that epidermal sensitization to penicillin may be frequently transient especially in the individuals who show mild reactions. According to Feinberg[4] allergic reactions from topical penicillin have been so numerous that this route of administration has been virtually abandoned. However, in the same article he points out that it has not been established that the incidence of reactions is significantly affected by the route of administration, by the type of penicillin, by the medium in which it is administered or by the addition of antihistamines. Keefer[17] states that the lowest incidence of reactions is associated with oral therapy and that the incidence is higher in those who have penicillin applied to inflamed skin.

The question of penicillin sensitivity is further complicated by the different types of penicillin available. There is no general agreement as to whether one type of penicillin can be tolerated when another cannot be tolerated. Feinberg[4] doubts whether there is a distinct specificity to the different types of penicillin. He suggests that much of the opinion that such a difference in antigenicity and specificity exists is based on observations on the ability of a patient to tolerate one type of penicillin after an allergic reaction has resulted from another type. However, frequently penicillin is tolerated with impunity after a previous "serum sickness" from the same type of drug. In a patient who had two prolonged reactions to penicillin G, both penicillin G and O gave skin reactions in the same high titre. Using delayed skin tests as their criteria, Risman and Boger[19] demonstrated considerable cross reaction between penicillins G, BT and O. In a recent report, Simon[21] discusses hypoallergic penicillin and when pyribenzamine in a concentration of 1 per cent was added to potassium penicillin G, reactions occurred in only 0.24 per cent of 1,237 patients.

An ideal answer to the question of penicillin hypersensitivity would be the development of a satisfactory skin test to be given routinely to all patients prior to receiving therapeutic penicillin to determine whether or not the drug can be tolerated. A review of the literature on this subject leaves the answer far from settled. Not only is there no general agreement on the reliability of the immediate and delayed skin tests, but there is also disagreement as to the importance of the different types of skin

tests—patch, scratch and intradermal. Peck,[15] with a series of 500 cases, concluded that the patch test is entirely unreliable for evaluating penicillin dermal sensitivities. Reyer[18] also states that patch tests are inconclusive. Peck[15] and Risman and Boger[19] claim that there is a significantly higher incidence of delayed skin reactions among those who have had allergic reactions to penicillin, and that the delayed skin reaction has some value in forecasting the likelihood of systemic reactions from its administration. Feinberg[4] states that immediate positive reactions to penicillin are rare but that in contact dermatitis from penicillin the patch test is usually positive. He also feels that history and observation are the main criteria by which diagnoses of penicillin sensitivity must be made rather than relying on skin tests. As a basis for this he points out that he has been unable to find antibodies transferable to man in the serum of patients sensitive to drugs which fail to give a positive skin test and that precipitins or transferable antibodies have not been found in connection with penicillin allergy.

Editorially[3] the *Journal of Allergy* discusses skin testing as follows:

"Further studies will be needed to establish the actual value of skin tests and to determine a technique of testing which will be sufficiently sensitive to yield reliable results without in itself producing dangerous reactions. Present indications are that scratch tests with solutions containing 10,000 to 50,000 units of crystalline penicillin per cc or intracutaneous tests with 0.01—0.02 ml of solution containing 100 to 1,000 units per cc might serve the purpose. Suspensions of procaine penicillin in oil or water are apparently not useful for skin tests."

Friedlaender and Friedlaender[6] feel that the reliability of skin tests as an indicator of penicillin sensitivity is generally insufficient for routine clinical use. Keefer[17] also feels that skin tests are unreliable in determining penicillin sensitivity. Schiller's[17] method of testing is to do a scratch test first using 1,000 units per cc followed by an intracutaneous test using 0.03—0.05 cc containing 10,000 units/cc. The immediate reaction is read and then the delayed reaction is read at twenty-four, forty-eight and seventy-two hours. He believes that the immediate reactions (scratch and intradermal), have a high degree of clinical sensitivity and that delayed reactions indicate some degree of clinical sensitivity. Sherman[17] believes that a negative reaction is not a reliable index that the patient is not sensitive as a negative reaction is often obtained even after a systemic reaction. Siegal[17] has found a positive delayed test in 5 per cent of adults who have never had penicillin but in about 50 per cent of those who have had reactions to penicillin.

In an attempt to assess the incidence of penicillin sensitivity in children we have searched for reactions to penicillin at the Hospital for Sick Children, Toronto, where there are approximately 18,000 indoor admissions and 83,000 outpatient admissions each year. In a representative week in 1953 a total of approximately 1,600 injections of penicillin were given to 224 patients. In spite of the great amount of penicillin used, we

have been able to find only three reactions which we feel can be definitely attributed to penicillin sensitivity, although we have found five other probable reactions and sixteen possible reactions which we could not substantiate by a study of the hospital records. Such statistics have obviously great disadvantages. Reactions may have occurred and not been recognized as such, reactions may have been recognized but not listed in the cross-index of the Medical Record Room, attending physicians who have been questioned may have forgotten mild reactions in their private patients and many patients were not followed long enough for delayed reactions to be observed. However, these statistics confirm the impression of many pediatricians that reactions to penicillin are rare in children and we can state with assurance that no anaphylactic reactions to penicillin, fatal or non-fatal, have occurred in patients in this hospital. Brief reports of our three cases follow.

Case 1.—A five-year-old white boy suffering with sore throat and fever was treated elsewhere with penicillin lozenges and intramuscular penicillin on the third day of his illness. On the fourth day of illness, the day he was admitted to hospital, his symptoms were worse and a red blotchy rash appeared on the face and spread to the neck, ears, hands and feet. Subsequently, although no further penicillin was given, a purulent conjunctivitis, swelling of the lips and ulceration of the pharynx developed. The rash then became bullous and marked photophobia appeared. Later a severe bilateral cicatricial entropion developed for which operation was required.

Two years previously he had had oral penicillin and one year previously intramuscular penicillin without untoward effect. There was no previous history of allergy.

Scratch and intradermal tests carried out, in the same manner as on the 200 patients described below, fifteen months after the onset of his illness were all negative. At the time of the skin testing there was still some residual photophobia and he had had to remain out of school for a whole year.

Case 2.—A six-year-old white boy with nasopharyngitis was treated elsewhere with intramuscular penicillin. Two hours later a generalized urticarial eruption developed and persisted, being so severe seven days later that admission to hospital was necessary. The urticaria persisted another seven days in spite of hospitalization and during this time the patient also suffered high fever, irritability, headache and nuchal rigidity. Lumbar puncture was negative.

Two years previously he had received intramuscular penicillin on five separate occasions without untoward effect. There was no previous history of allergy.

After two weeks in hospital he was completely cured. The parents refused to allow skin testing.

Case 3.—A seven-year-old white boy suffering with acute tonsillitis and cervical adenitis was treated elsewhere with intramuscular penicillin for three days. Fifteen days later he had generalized giant urticaria, high fever, pains in the arms and legs, pain on flexion of the neck and abdominal pain, for which hospitalization was required. The symptoms lasted only four days in the hospital and he was discharged cured.

He had received penicillin on many occasions previously, the last time one year prior to the above illness. There was no previous history of allergy. The parents refused to allow skin tests to be done.

TABLE III. INCIDENCE OF PENICILLIN SENSITIVITY REACTIONS IN 600 CHILDREN

	Age	Total Number	Number Who Had Received Penicillin Without Reaction	Number Who Had Received Penicillin With Reaction			Per Cent of Definite Reactions	Per Cent of Total Reactions
				Definite Reaction	Probable Reaction	Possible Reaction		
Non-allergic group	0-1 yr.	69	67			2-rash		
	1 yr.	89	85	1-angioneurotic edema		1-urticaria 1-exacerbation of rash 1-rash		
	2-5 yrs.	252	249	1-angioneurotic edema + urticaria		1-rash 1-puffy eyes	0.6%	2%
	6-10 yrs.	99	98	1-urticaria				
	11-14 yrs.	6	6					
Total		515	505	3	0	7		
Allergic Group	0-1 yr.	0						
	1 year	5	5					
	2-5 yrs.	37	33	1-arthralgia & purpura 1-urticaria	1-urticaria	1-vomiting		
	6-10 yrs.	32	31	1-arthralgia & urticaria			6%	8%
	11-14 yrs.	11	9	1-exacerbation of existing atopic dermatitis 1-urticaria				
Total		85	78	5	1	1		

Of these three cases only *Cases 2* and *3* are extremely convincing as cases of penicillin sensitivity. However, the most serious, *Case 1,* was studied intensively and no other explanation of the clinical picture could be advanced by the attending staff, who felt that this was definitely a case of penicillin sensitivity.

To further assess the incidence of penicillin sensitivity in children records of private patients of one of us (CCW) were searched. The records were selected from the file alphabetically, the only criterion being that the patient had previously received penicillin at least once. In each case the parents were questioned as to any reactions following the penicillin. There were a total of 600 patients (Table III), 515 of whom are described as "nonallergic" since they were seen for general pediatric care and did not have a complaint of a major allergy (eczema, urticaria, hay fever or asthma). The remaining eighty-five are described as "allergic" because they were seen for a major allergy. Reactions are divided up into definite, probable, and possible according to the best assessment which we could make as to whether the symptoms described by the parent could be attributed to penicillin sensitivity. From a study of the table it is at once apparent that the incidence of reactions is much greater

in the allergic group, even if the evidence is weighted in favor of the nonallergic group by including the seven possible reactions.

In an effort to further clarify penicillin skin tests, 200 children were each tested by scratch and intracutaneous tests in the following manner: scratch tests using aqueous crystalline penicillin* 10,000 units/cc and 50,000 units/cc and intracutaneous tests using 0.02 cc of each of trichophyton 1:1,000 dilution, penicillium notatum 1:1,000 dilution, penicillium mixture 1:1,000 dilution, aqueous crystalline penicillin 100 units/cc and aqueous crystalline penicillin 1,000 units/cc, were done on each patient. (Table IV). Two-thirds of this group were "nonallergic" children chosen at random from the indoor and outpatient departments of the Hospital for Sick Children and who had no history of major or minor allergy. The remaining one-third of the group were allergic children who were attending the Allergy Clinic of the Hospital for Sick Children for treatment of a major allergy. In the "nonallergic" group sixty-eight had received penicillin previously, thirty-two had not received it previously and thirty-three were receiving it for the first time when the skin testing was performed. For the allergic group these figures were fifty-three, thirteen and one, respectively.

None showed reactions to penicillin by scratch test, three showed reactions by intracutaneous test. Of these three patients two had had previous penicillin and were also receiving penicillin at the time of testing. The third had never received penicillin but also gave positive tests with molds. None of the three was clinically sensitive to penicillin.

Certain differences in the positive skin tests between these two groups are noted. Many positive reactions were obtained with the moulds. These occurred in the allergic group twice as frequently as in the nonallergic group. There was no significant difference in the reactions to penicillin in the two groups. No correlation was found between reactions to the molds on the one hand and penicillin on the other.

It may be inferred from the negative results in this study that the materials which were being used for testing were inactive with regard to their ability to induce positive skin tests. With this in mind we performed these same tests on seven adults on the staff of the hospital, all of whom were known to be clinically sensitive to pencillin, and obtained positive reactions in three.

Case 1.—A twenty-one-year-old nurse had several injections of penicillin two years previously. One year previously, after a single injection of SR penicillin, a large indurated local reaction developed at the site. Six months previously another injection of penicillin resulted in urticaria and nausea and subsequently oral penicillin resulted in sneezing and coughing. This patient showed a markedly positive scratch test with the 10,000 units/cc dilution.

Case 2.—A twenty-seven-year-old intern had had several injections of penicillin previously, and subsequent to his last injection, two years before skin testing, suf-

*Kindly supplied by Parke-Davis Co. Lot No. KWG-7512—99.7 per cent pure.

TABLE IV. RESULTS OF SKIN TESTS WITH PENICILLIN AND RELATED MOULDS PERFORMED ON 200 CHILDREN

		Scratch Tests						Intracutaneous Tests										Total Number of Patients	Number with Present or Previous Fungus Infections
		Penicillin 10,000 u/cc		Penicillin 50,000 u/cc		Control		Trichophyton 1:1000		Pen. Notat. 1:1000		Pen. Mix. 1:1000		Penicillin 100 u/cc		Penicillin 1000 u/cc		Control			
		I	D	I	D	I	D	I	D	I	D	I	D	I	D	I	D	I	D		
Non-allergic group																					
0-1 yrs. inclusive	44	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	108	11
		−	−	−	−	−	−	+	−	+	−	+	−	−	−	−	−	−	−	8	1
2-5 yrs. inclusive	35	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	3	
		−	−	−	−	−	−	+	+	−	−	−	−	−	−	−	−	−	−	2	
6-14 yrs. inclusive	54	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	2	
		−	−	−	−	−	−	+	−	−	−	+	−	−	−	−	−	−	−	1	
Total	133	−	−	−	−	−	−	++	−	++	−	++	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	+	−	+	−	+	−	+	−	+	−	−	−	1	
		−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	+	−	+++	−	+	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	1	1
		−	−	−	−	−	−	−	−	+	−	+	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	++	−	−	−	−	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	−	+	−	+	−	+	−	−	−	−	−	−	1	1
		−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	1	
Allergic group		−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	43	
		−	−	−	−	−	−	+	−	+	−	+	−	−	−	−	−	−	−	9	1
0-1 yrs. inclusive	5	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	2	
		−	−	−	−	−	−	+	−	++	−	+	−	−	−	−	−	−	−	2	
2-5 yrs. inclusive	14	−	−	−	−	−	−	+	−	−	−	+	−	−	−	−	−	−	−	2	
		−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	1	
6-14 yrs. inclusive	48	−	−	−	−	−	−	+	−	+	−	−	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	++	−	++	−	++	−	−	−	−	−	−	−	1	
Total	67	−	−	−	−	−	−	++	−	−	−	−	−	−	−	−	−	−	−	1	1
		−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	++	−	+	−	−	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	−	−	−	−	++	−	−	−	−	−	−	−	1	
		−	−	−	−	−	−	−	−	−	−	−	−	−	−	+++	−	−	−	1	
		−	−	−	−	−	−	+++	−	+++	−	+++	−	−	−	−	−	−	−	1	

I—Immediate reaction—read at 10-20 minutes.
D—Delayed reaction—read at 48 hours.

fered generalized urticaria requiring hospitalization. He had a positive intracutaneous skin test with the 100 units/cc dilution.

Case 3.—A twenty-year-old nurse suffered dermatitis, swelling of the eyelids, nausea and chills if she handled penicillin. She showed a positive delayed (twenty-four hours) intracutaneous test with the 100 units/cc dilution.

Case 4.—A twenty-five-year-old nurse, one year previously, after a single injection of penicillin (she had had penicillin previously) suffered urticaria, arthralgia, and angioneurotic edema of the eyelids. Skin tests were negative one year later.

Case 5.—A thirty-six-year-old nurse had handled penicillin frequently but had never received it therapeutically until she received one injection which resulted in angioneurotic edema of the eyes. Skin tests were negative eight months later.

Case 6.—A thirty-three-year-old nurse took occasional penicillin lozenges for sore throat. Once she suffered angioneurotic edema of the eyes following the application of penicillin ointment to the wrist, and later, following application of penicillin ointment to an infected area of skin suffered a generalized morbilliform rash and very severe angioneurotic edema of the eyelids. Skin tests negative one year later.

Case 7.—A twenty-six-year-old nurse had received single injections of SR penicillin on two occasions over a two-year period. A third injection resulted, within five minutes, in an acute anaphylactic reaction with difficult breathing, hoarse voice, itching of the scalp, facial urticaria, and angioneurotic edema of the eyes. Rapid improvement followed the immediate injection of adrenalin. Skin tests one year later were negative.

DISCUSSION

The above findings together with the scanty reports in the literature on penicillin sensitivity in children confirm the impression of most pediatricians that reactions to penicillin are rare in children. It will be noted that while exhaustive search revealed only three children with clinical penicillin sensitivity in a large hospital where thousands of children receive thousands of injections of penicillin each year, we had no difficulty in finding several adults on the staff of that same hospital who were definitely clinically sensitive to penicillin and could have given several more case reports than we did.

The figures on the nonallergic group of private patients also indicate a very low incidence of reactions (0.6 per cent definite reactions). However, the figure of 6 per cent definite reactions in the allergic group of private patients is in striking contrast to this and should considerably modify any tendency to use the drug indiscriminately in allergic children. Nor should this low incidence of reactions in nonallergic children lull us into a false sense of security. Sensitivity reactions to penicillin do occur in children, some of these are quite serious and already one fatal anaphylactic reaction has been reported in the literature. Moreover, the widespread use of penicillin in the children of today may result in large numbers of sensitivity reactions in the adults of tomorrow.

For these reasons it is extremely important to govern our use of penicillin accordingly. No patient should be given penicillin unless there is

a positive indication for the use of that drug. If chemotherapy is indicated for a relatively mild infection, some other suitable antibiotic should be used if possible, reserving penicillin, our best antibiotic agent, for the more severe infections, particularly those in which intramuscular therapy is necessary. The drug should be used orally if possible, intramuscular use being reserved for indications like vomiting or very acute illness. Before the drug is administered by any route a history should be taken of previous administration and any reactions resulting from its use. If a reaction has occurred in the past, the indications for using the drug again should be carefully re-evaluated.

Our own findings and the findings of many others referred to above indicate that skin tests are of very limited value. Unfortunately we succeeded in skin testing only one of our three sensitive children admitted to the hospital, with negative results. Of the seven adults reported here only three gave positive skin tests and it is interesting to note that they were negative in the one patient who had had an acute anaphylactic reaction one year previously. This is in contradiction to Feinberg's[5] statement that it is practically a certainty that the skin test will be positive in those persons who react anaphylactically to penicillin.

Our own skin tests confirm the findings in the literature that there is no correlation between skin tests with penicillin and those with penicillium and related molds. Our finding of an increased incidence of reactions to molds in the allergic group is to be expected since many of these children were known to react to other molds also.

If an anaphylactic reaction to penicillin does occur it must be treated promptly. According to Feinberg,[5] at the first sign of an immediate anaphylactic reaction 0.5 to 1.0 cc of epinephrine in 1 :1,000 dilution should be given intravenously, followed in two or three minutes by a similar dose if no improvement is seen. As soon as this has been administered, aminophylline 3.75 grain in 10 cc fluid should be given intramuscularly. Oxygen should be administered for cyanosis and plasma for shock.

CONCLUSIONS

1. The literature on penicillin sensitivity has been briefly reviewed. The reported incidence of reactions varies from 2 to 10 per cent. Many types of reactions have been reported, chiefly skin rashes, but fourteen acute anaphylactic deaths have been reported and we have referred to two more not previously reported.

2. Penicillin sensitivity reactions in children are very rare as shown by a review of the literature and a review of the children seen at the Hospital for Sick Children, Toronto. We have found only three cases in children in this hospital, though several more in adults on the hospital staff. However, it is not rare in allergic children as shown by our incidence of 6 per cent in private allergic patients.

3. Skin testing has little value in an evaluation of penicillin sensitivity.

A determination of penicillin sensitivity depends on the history of previous administration of the drug and any reactions which resulted. While a positive skin test probably indicates sensitivity, a negative skin test does not mean lack of sensitivity.

4. There is no correlation between positive skin tests with penicillin and those with the penicillium molds.

REFERENCES

1. Brown, E. A.: Reactions to penicillin. (A Review of the literature 1943-1948.) Ann. Allergy, 6:723-746, 1948.
2. Curphey, T. J.: Fatal anaphylaxis in bronchial asthma following administration of penicillin. Reported at the 1952 March meeting of the Am. Academy of Forensic Sciences.
3. Editorial: Fatal allergic reactions to penicillin. J. Allergy, 23:383-384, 1952.
4. Feinberg, S. M.: Drug allergy—some clinical and immunological aspects. Ann. Allergy, 10:260-269, 1952.
5. Feinberg, S. M.; Feinberg, A. R., and Moran, C. F.: Penicillin anaphylaxis, nonfatal and fatal reactions. J.A.M.A., 152:114-119, 1953.
6. Friedlaender, A. S., and Friedlaender, S.: Cutaneous manifestations of drug hypersensitivity. Quart. Rev. Allergy, 6:54-67, 1952.
7. Goltman, J. S.: Mechanisms of penicillin reaction. Ann. Allergy, 10:278-281, 1952.
8. Harpman, J. A.: Death from penicillin. Brit. M. J., Correspondence, 392 (Aug. 16) 1952.
9. Higgins, G. A., and Rothchild, T. P. E.: Fatal anaphylactic shock from procaine penicillin. New England J. Med., 247:644-646, 1952.
10. Hopkins, J. G., and Lawrence, H.: Sensitization to penicillin. J. Allergy, 18: 251-262, 1947.
11. Keefer, C. S.; Blake, F. G.; Marshall, E. K., Jr.; Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in the treatment of infections. A report of 500 cases. J.A.M.A. 122:1217-1224, 1943.
12. Lepper, M. H.; Dowling, H. F.; Robinson, J. A., and Stone, T. E.: Studies in hypersensitivity to penicillin. Incidence of reactions in 1,303 patients. J. Clin. Investigation, 28:826-831, 1949.
13. Levin, S., and Moss, S. S.: Injections in allergic children. Ann Allergy, 9: 471-476, 1951.
14. Mayer, P. S.; Mosko, M. M.; Schutz, P. J.; Osterman, F. A.; Steen, L. H., and Baker, L. A.: Penicillin anaphylaxis. J.A.M.A,, 151:351-353, 1953.
15. Peck, S. M.; Siegal, S.; Glick, A. W., and Kurton, A.: Clinical problems in penicillin sensitivity. J.A.M.A., 138:631-638, 1948.
16. Peck, S. M., and Hewitt, W. L.: The production of an antibiotic substance similar to penicillin by pathogenic fungi (dermatophytes). Pub. Health Rep., 60:148-153, 1945.
17. Reported at the 1953 Annual Meeting of the American Academy of Allergy.
18. Reyer, W. A.: A Study of the pathogenesis and classification of dermatologic penicillin reactions. Ann. Allergy. 10:270-277, 1952.
19. Risman, G., and Boger, W. P.: Human skin sensitivity to penicillin G, BT and O. Demonstration of cross-sensitization. J. Allergy, 21:425-431, 1950.
20. Siegal, S.; Steinhardt, R. W., and Gerker, R. G.: Fatal and near-fatal penicillin anaphylaxis. J. Allergy, 24:1-19, 1953.
21. Simon, S. W.: Hypoallergic penicillin V (Pyribenzamine-Penicillin) Comparison of results and final conclusions from all studies. Ann. Allergy, 11:218-221, 1953.
22. Smith, W. S., and Walker, A. D.: Penicillin Decade (1941-1951) Washington, D. C.: Arundel Press, Inc., 1952.
23. Thomson, W. O.: Sudden death following an injection of penicillin. Brit. M. J., 70-75 (July 12) 1952.
24. Waldbott, G. L.: Anaphylactic death from penicillin. J.A.M.A., 139:526-527, 1949.
25. Wilensky, A. O.: Fatal delayed anaphylactic shock after penicillin. J.A.M.A., 131:1384, 1946.

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ANAPHYLAXIS TO PENICILLIN

Report of an Unusual Case

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THE CASE which is to be presented is not a medical oddity. It exemplifies one of the basic and more terrifying allergic reactions which can be observed—anaphylactoid shock, in this instance due to penicillin. It is a syndrome which is being seen more frequently all the time. It seems hardly possible that more penicillin can be given indiscriminately than is now being given, but the percentage of cases of sensitivity may increase as more of the population receive sensitizing doses.

Surely there are many more examples similar to this case which have not found their way into the literature as yet. Only eleven cases[1,2,4,7] had been reported at the time this paper was started but since then twenty-three more[4,5,6] have appeared, including fourteen which were due to Penethamate Hydriodide (Neo-Penil). In all, six deaths have occurred. The clinical picture in most of the cases has presented a striking similarity, including: sensitizing injections with the antigen (penicillin), variable latent period, subsequent injection with onset of anaphylactoid reaction appearing within a matter of seconds or a very few minutes at the most. Substernal oppression, respiratory difficulty, urticaria at times, and circulatory collapse were observed in almost all the patients.

Case 1.—The patient whom I shall discuss was a white, married woman, nineteen years of age. She was admitted because of severe circulatory collapse. She had received 300,000 units of penicillin (type unknown) in the office of her family physician. The reason for her receiving the injection could not be determined definitely. About three or four minutes later she sneezed violently twice, experienced immediate pelvic pain and went into shock. Her physician sent her to the hospital immediately.

On admission the patient was slightly cyanotic; her pulse was about 160 as counted at the apex, and no peripheral pulse could be felt nor could her blood pressure be obtained. There was massive angioneurotic edema of both lips. There was no asthma. Her abdomen was soft. A blood count taken in the emergency room revealed marked hemoconcentration, the red count being 7,000,000, the hemoglobin 20 gm (130%), and the white count 50,000. No eosinophil cells were seen.

It was felt that she had a severe anaphylactic reaction to penicillin. She had had penicillin prior to this injection on several occasions. The possibility of an ectopic pregnancy with rupture was entertained, particularly in view of her having had no menstrual periods for the previous four months, and she was seen in consultation by a member of the gynecological department before she was taken to her room. He found some enlargement of the uterus but no signs pointing to a ruptured ectopic pregnancy.

She responded to shock therapy slowly during the night. She received epinephrine

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(1-1,000) .5 cc subcutaneously and 1,000 cc 10 per cent dextrose in water intravenously. Blood was crossmatched but not given since she was improving steadily. She was in good condition before morning. Her chest remained clear. The angioneurotic edema had disappeared completely. Her abdomen was still soft, but she showed a slight hemorrhagic discharge from the cervical os. Her blood count that morning showed 4,390,000 red cells, 14.2 gm of hemoglobin and 20,950 white cells. No eosinophils were reported on the differential. The consultant felt that it was safe for her to go home the following day in view of no further appearance of abnormal pelvic signs.

Three days later, however, the patient was readmitted to the gynecological service with severe lower abdominal pain. A laporotomy revealed a ruptured left tubal pregnancy with approximately 1,000 ml of blood in the peritoneal cavity. The convalescence was normal.

This patient differed from other reported cases in that an ectopic pregnancy complicated the picture. It seems more than mere coincidence that her tubal pregnancy ruptured within five days of her penicillin reaction, and it probably would be a safe assumption that some alteration in the circulatory supply of the fallopian tube brought on by the shock hastened its rupture. Possibly a small amount of bleeding started coincident with the shock episode. In retrospect it is felt that the immediate circulatory collapse was not due to the ectopic pregnancy, even though it was a confusing possibility at first.

Another point should be emphasized here: the rapidity of onset of the symptoms. This would indicate that the penicillin was inadvertently given intravenously. No other explanation could account for such abrupt initiation of circulatory collapse. In all the cases reported it was concluded that a similar accident occurred.

Reactions to penicillin fall into three categories: (1) the urticarial or serum-sickness syndrome which can be most annoying, uncomfortable and prolonged but which is not fatal, (2) the various dermatologic types which can be more serious and even fatal, and finally (3) the anaphylactoid reaction. From a numerical standpoint they occur in decreasing order of frequency. The number of urticarial reactions is rapidly on the increase, and it can be anticipated that they will become more severe as well. The dermatologic types are including more cases of exfoliative dermatitis now. Only recently has interest been focused on the anaphylactoid reactions.

The mechanism of the latter reaction has never been explained adequately. Precipitins probably play the biggest role, and the other antibodies — heterophile antibodies, atopic reagins, blocking antibodies, hemolyzing antibodies and the others — probably do not enter the picture. But just how they cause the reaction is not clear. Even though present, they will not effect anaphylactoid shock unless there has been intermittent administration of the antigen just as in anaphylaxis produced in animals. Hence the first injection in a series is the only one likely to produce anaphylactoid shock.

Prevention of this syndrome is theoretically possible. Siegal[6] and his co-workers emphasized certain precautionary measures: (1) avoidance of unnecessary injections when oral medication is equally effective, (2) careful questioning as to previous penicillin sensitivity or other allergic manifestations, (3) consideration of skin-testing with penicillin prior to injection, and (4) greater care in the actual injection itself.

SUMMARY

The case of a young woman with an ectopic pregnancy who experienced a severe anaphylactoid reaction to penicillin is presented to emphasize the seriousness of this syndrome and the increasing frequency of this type of penicillin reaction.

ACKNOWLEDGMENT

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BIBLIOGRAPHY

1. Brown, E. A.: Progress in Allergy. Reactions to penicillin. A review of the literature, 1943-1948. Ann. Allergy, 6:723-746 (Nov.-Dec.) 1948.
2. Burleson, R. J.: Anaphylactoid shock due to penicillin. J.A.M.A., 142:562-563 (Feb. 25) 1950.
3. Gordon, E. J.: Delayed serum sickness reaction to penicillin. J.A.M.A., 131: 727-730 (June 29) 1946.
4. Mayer, P. S.; Mosko, M. M.; Schutz, P. J.; Osterman, F. A.; Steen, L. H., and Baker, L. A.: Penicillin anaphylaxis. J.A.M.A., 151:351-353 (Jan. 31) 1953.
5. Report of Council on Pharmacy and Chemistry. Severe anaphylactoid and fatal reactions to penethamate hydriodide (Neo-Penil). J.A.M.A., 151:1105 (Mar. 28) 1953.
6. Siegal, S.; Steinhardt, R. W., and Gerber, R.: Fatal and near-fatal penicillin anaphylaxis. J. Allergy, 24:1-10 (Jan.) 1953.
7. Waldbott, G. L.: Anaphylactic death from penicillin. J.A.M.A., 139:526 (Feb.) 1949.
8. Wilensky, A. O.: Fatal delayed anaphylactic shock from penicillin. J.A.M.A., 131:1384 (Aug. 17) 1946.

115 W. Fairview Ave.

CHICAGO ALLERGISTS ELECTED TO OFFICE

Dr. Morris A. Kaplan of Chicago has been elected chairman of the Section of Allergy of the Illinois State Medical Society. Dr. A. L. Aaronson has been elected president of the Chicago Society of Allergy.

ALLERGIC PAROTITIS

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THE PURPOSE of this paper is to invite attention to the clinical entity Allergic Parotitis which has not been mentioned in any of our texts with the single exception of Hansel.[2]

Pearson[1] in 1935 reviewed the literature on the subject of recurrent parotitis and added eleven cases in which evidence of allergy was present as the cause of the attacks. In his review extending back to Kussmaul's[3] report in 1879, he found reports of cases by Vogeler,[8] Burton-Fanning,[1] and Meyer.[4] In 1936, Pearson[6] added two more cases of his own bringing the total reported to that date to seventeen cases.

Since 1936, eight more cases have been found, one by Sein[7] (the youngest reported, two and one-half years), one by Zindler and Fraser[10] and three by Serafini. Waldbott,[9] reported three cases and I, in this report, add one bringing to date a total of twenty-six cases of which I have knowledge.

CASE REPORT

Case 1.—Mrs. V. S. J., aged thirty-one, presented herself at the office June 13, 1949, with a chief complaint of recurrent swelling of the parotid glands, some attacks unilateral, one side or the other, other attacks bilateral, of nine years' duration, occurring at intervals varying from one week to three months. During this nine-year period she had perennial hayfever with much eye discomfort consisting of itching and sense of swelling of the globe. Also, during this time she had recurrent ureteral blockage (which her urologist suggested was on an allergic basis) and anal itching. Her only food suspicions were black pepper and "sweets." Her father has asthma and hay fever.

She came in with a swollen left parotid gland. I stripped out her parotid duct and obtained a clear thick jelly-like cast which contained 100 per cent eosinophiles. Her physical examination was otherwise negative except a nasal mucous membrane pale and wet, a smear of which revealed 20 per cent eosinophiles. Blood count and urinalysis were normal. Skin tests gave moderate to strong reactions to nine of our major pollens with negative reactions to molds, house dust, grain dusts, and danders. To foods she gave strong reactions to wheat, potato, cottonseed, all beans and peas and grapefruit. Subsequently, a week after her swelling had disappeared on a skin negative diet, her positive reacting foods were added back one at a time each three days. All were without clinical significance except wheat which was followed in two hours by an attack of parotid swelling and in twenty-four hours by anal itching. She was placed on a wheat-free diet and hyposensitization for her hay fever. She was discharged from treatment at the end of the ragweed season in 1951, with freedom from subsequent symptoms except on three occasions when wheat was tried, each time followed by parotid swelling, each attack bringing out salivary eosinophilia not present otherwise. Subsequent to discharge she reported on June 4, 1952, she used wheat in considerable quantity for two days and had an attack. December 9,

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1952 (two and one-half years after my first observation of her), she reported that she was tolerating wheat very well in moderation but that considerable amounts would produce excessive flow of saliva without swelling of the glands and that she has occasional mild hay fever.

Pattern of allergic parotitis: Usually a personal and/or family background of allergy; recurrent attacks of unilateral or bilateral swelling of the parotids; thick ropy sputum that often forms plugs or casts of the duct; sputum contains many eosinophiles; attacks are precipitated by specific allergens, inhalant or ingested, and are relieved and prevented by avoidance or hyposensitization.

Conclusion: allergic parotitis is a clinical entity of infrequent occurrence worthy of notice in our medical texts.

BIBLIOGRAPHY

1. Burton-Fanning, F. W.: Periodic Swelling of the Salivary Glands. Brit. M. J., 2:517, 1925.
2. Hansel, French K.: Clinical Allergy. St. Louis: C. V. Mosby Co., 1953.
3. Kussmaul, I.: Anfallsweise Auftretende Speichelgeschwulst in Folge von chronischer eitrig fibrinoser Entzundung des Stenonschen Ganges. Klin. Wchnschr., 60:209-211 (Apr. 14) 1879.
4. Meyer, H. S.: Chronic Sialodochitis. J. Pediat., 4:248-250, 1934.
5. Pearson, R.S.B.: Recurrent swelling. Arch. Dis. Childhood, 10:363-376 (Oct.) 1935.
6. Pearson, R. S. B.: Two cases of Recurrent Swelling of the Parotids. Guy's Hosp. Rep., 86:333-342 (July) 1936.
7. Sein, M.: Recurrent swelling, with report of case: two-and-one-half-year-old Burmese child believed to be allergic. Indian M. Gaz., 72:526-528 (Sept.) 1937.
8. Vogeler, K.: Uber die chronische Entzundung der Parotis. Arch. f. klin. Chir., 122:655-663, 1922-25.
9. Waldbott, George L.: Allergic Parotitis. J. Allergy, 18:51 (Jan.) 1947.
10. Zindler, G. A., and Fraser, R. H.: Allergic swelling: forty-two-year-old woman sensitive to turkey feathers. J. Michigan M. Soc., 47:863-868 (Aug.) 1948.

Medical Arts Building

SECTION ON ALLERGY ELECTS OFFICERS

At the recent meeting of the Section on Allergy of the Medical Society of the County of Kings and Academy of Medicine of Brooklyn, the following officers were elected:

President—Harry Markow, M.D.
Vice President—Arthur William Grace, M.D.
Secretary—Harry Leibowitz, M.D.
Treasurer—Solomon Slepian, M.D.

The following were elected as members of the Executive Committee: Richard H. Bennett, M.D., Dorothea Curnow, M.D., Harold Dundy, M.D., Louis Levin, M.D., George A. Merrill, M.D., William Messer, M.D., Emanuel Schwartz, M.D., Benjamin Zohn, M.D.

ASTHMA IN INFANCY

WILLIAM P. BUFFUM, M.D., F.A.C.A.
Providence, R. I.

THERE is disagreement as to the allergenic agents responsible for the manifestations of asthma in infancy. In this paper is presented evidence that inhalants and foods play the same part in infancy that they do in older children, and that infection is an additional factor.

This study has been made by reviewing the records of thirty private patients seen with a diagnosis of asthma before one year of age. Two records were omitted because the patients were seen only once, otherwise the records are unselected.

In attempting to demonstrate the extrinsic nature of these cases, and the multiple allergies which they have, some data from case histories are presented. The positive scratch tests have been recorded, and also the clinical sensitivities as shown in the histories and by feeding tests.

It is not claimed that the clinical sensitivities are reported correctly in every individual case. In the histories we are dependent on the observations of the mother, and in the feeding tests, which were carried on at home, mistakes may have been made. However, an effort has been made to be conservative, and it seems clear that most of the clinical sensitivities are correctly recorded.

Case 1.—J. B. as seen at eight months of age.

Positive Scratch Tests.—He had a one plus reaction to cat, dust, wheat, egg, spinach, and potato.

Clinical Sensitivities Demonstrated.—Wheezing respirations resulted from dust, egg, wheat, spinach, and potato. Cod liver oil, potato, beets, and orange juice induced vomiting.

Discussion.—John is the only one of the thirty patients with a positive scratch test to dust. Clinically he is extraordinarily sensitive to dust. This case and the others suggest that at this age a high degree of sensitivity or a prolonged period of sensitivity is necessary to produce a positive skin test to dust.

Case 2.—Sally H., seen at seven months of age. Patient relieved without injections.

Positive Scratch Tests.—She has slight positive tests to orris and penicillin.

Treatment.—She had six hairy stuffed toys in the crib with her. These were removed. She was also to be protected from dust and toilet powder. No dietary change was made. Orange juice which gave her a rash had already been omitted.

Results.—A letter states that two days after removal of the stuffed toys she was well and that she has remained so for five years.

Discussion.—We were not able to prove anything in this case. However, it seems almost certain that the asthma was relieved by the removal of stuffed and hairy toys. Like all but one of the others, she had a negative test to house dust. Although

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she had only two faintly positive tests, she seems to be an extrinsic case, sensitive to dusts and at least one food, orange.

Case 3.—Billy B., five months old, had a mild caes of asthma.

Skin Tests	5 months	1½ years	4 years
Timothy	0	+ -	+
Ragweed	0	0	+
Aspergillus	0	0	+
Hormodendron	0	+	0
Penicillium	++	0	0
Mustard		+	
Silk		+	

Clinical Sensitivities Demonstrated.—None.

Discussion—The cause of his asthma (except for a respiratory infection) was not clearly demonstrated.

It is interesting to watch the development of pollen hay fever in which the skin tests paralleled the clinical symptoms.

Case 4.—Arthur C., nine months old, had a severe case of asthma.

Positive Scratch Tests.—

	10 Mos.	11 Mos.	2½ Yrs.	4 Yrs.	5 Yrs.	6 Yrs.	6½ Yrs.
Horse		+	0	0			
Feathers	0	+	0	0			
Orris		+	0	0			
Cottonseed		0	++++	0	+		
Kapok		0	0	0			
Dust	0	0	0	+			
Oak						++	
Birch						++	
Timothy		0	0	+++	0	+++	
Ragweed	0	0	0	0	++	+++	
Alternaria		0	0	+	+++	+++	
Aspergillus		0	+++	0			
Hormodendron		++	0	+	0	+	
Egg	+++	+++	+++				+++
Beef	+						0
Chicken			+++				0
Peas	0	+					0
Spinach	0		0				++
String bean	0	0					+
Salmon	0		+				0
Rice	+		0				0
Corn	0		+				+

Clinical Sensitivities Demonstrated.—To egg, orange, and possibly milk.

Discussion.—Although the wheezing now occurs mostly in the colder weather with respiratory infections, he had several demonstrated clinical sensitivities. He has developed positive skin tests to several pollens but as yet no seasonal asthma or hay fever has been noted.

Case 5.—Gayle S., seven months old, had food allergies.

	Scratch Tests.— 7 Mos.	2 Yrs.	3½ Yrs.
Cottonseed	0	+	0
Penicillium	+	0	0
Chicken	+	0	
Spinach	++	0	
Cornmeal	0	+	

Clinical Tests.—Egg, wheat, and milk induced cough. Orange juice, egg, lamb, lima bean, spinach, and potato caused vomiting. The injection of Penicillin induced wheezing.

Case 6.—Louis Z., eight months old.

Scratch Tests.—	Oct. 21, 1949	Oct. 2, 1951
Aspergillus	+	0
Alternaria	+	0
Chicken	+	
String bean	+	
Potato	+	

Clinical Tests with egg, orange, and possibly potato resulted in wheezing.

Discussion.—In this case the mother is not reliable, and it is impossible to be certain of anything. Egg and orange seem to make him wheeze. Respiratory infections have been frequent and severe, but lately there has been no respiratory difficulty. This case we regard as asthma due to food allergies.

The records of six patients with entirely negative scratch tests were studied to see if there was any evidence as to whether these patients were allergic to inhalants and foods, or whether the asthma seemed to be infectious in character. The records of these six patients are briefly summarized below.

Peter B., six weeks old. He improved when out of doors, in the hospital, and was better at home after dust precautions has been instituted, and exaporated milk had been added to his diet.

Linda H., three months old. She is symptom free in her grandmother's house, better after using dust seal in her home, and improved after boiling milk for one-half hour. She vomits orange juice.

Rosemary D., six months old. She improved within a few days after taking dust precautions in her room, and was perfectly well for four months.

Virginia N., eight months old. She showed definite improvement after dust precautions and injections of dust and vaccine. At two years of age she had positive tests to rabbit, cottonseed, *dust*, timothy, and aspergillus.

Brian O., ten months old. The eczema was considerably improved without orange juice. His asthma seemed better on boiled skimmed milk.

David K., four months old. He had a rash on his face from orange juice. He was much better immediately after dust precautions, and injection of dust and vaccine.

DISCUSSION

As evidence this material is vague, and in each individual patient it is unsatisfactory. However, from reading the records one after the other, one gets the distinct impression that these patients suffer from extrinsic asthma due to inhalants and foods, and that the infectious element is of secondary importance.

The next three tables show the positive scratch tests and their relationship to clinical sensitivity. It should be recognized that the relationship shown is only what could be found in the records of patients being treated

TABLE I. POSITIVE SCRATCH TESTS—FIRST TESTING

Positive Tests in Thirty Patients

Spinach	10	Ragweed	2
Egg	7	Chicken	2
Aspergillus	6	Wheat	1
Alternaria	5	Milk	1
Penicillium	5	Cat	1
Hormodendron	4	Dog	1
Timothy	4	Cotton	1
Potato	4	Orris	1
Tomato	4	Silk	1
String bean	3	Dust	1
Orange	3	Beef	1
Salmon	3	Peas	1
		Mustard	1

TABLE II. POSITIVE SCRATCH TESTS TO FOODS

	Number of Positive Scratch Tests	Confirmed by Clinical Trial
Spinach	10	2
Egg	7	3
Potato	4	1
Tomato	4	0
Orange	3	3
String bean	3	0
Salmon	3	0
Chicken	2	0
Wheat	1	1
Milk	1	1
Beef	1	0
Peas	1	0

in the regular way. In some cases the patients were doing well and no great effort was made to demonstrate food allergies. In other cases, as for instance with egg sensitivity, frequently this was not demonstrated because it was inadvisable to bring on an attack.

COMMENT

It is interesting that there was only one positive test to house dust and that this occurred in a patient who was clinically exquisitely sensitive to house dust. This would suggest that with house dust, the clinical sensitivity antedates the skin sensitivity.

Only three of the positive egg cases were confirmed by clinical tests. This was because we did not try the clinical test for egg, fearing a serious reaction. Wheat and milk each gave one positive scratch test and this was confirmed by clinical test. Three positive scratch tests to orange were all shown to be significant. Positive tests to string bean, fish, chicken, lamb and peas, were all probably of no importance.

If as criteria we include vomiting, eczema or wheezing, orange gives many more clinical tests than scratch tests. Wheat and milk also give more clinical tests than scratch tests.

TABLE III. POSITIVE CLINICAL TESTS TO FOODS

	Number of Tests	Accompanied by Positive Scratch Tests
Orange	11	3
Egg	6	3
Wheat	4	1
Spinach	3	2
Milk	2	1
Beets	2	0
Potato	2	1
Fish	1	0
Beef	1	0
Lamb	1	0
Lima bean	1	0
Oats	1	0

At this age orange and egg would be important troublemakers, except for the fact that usually the mother has recognized this allergy herself.

Milk and wheat are less common sensitizers, but make more trouble because of the difficulty in making the diagnosis.

DISCUSSION

The more severe cases, as typified by four of the first five cases shown, are clearly sensitive to many substances, inhalants and foods. In the milder cases these multiple allergies are not clearly shown, but this by no means proves that they do not exist.

It has been easier to demonstrate sensitization to foods than to inhalants. Nevertheless, the reaction of these babies to environment is similar to that of older children. The few patients that were taken to the hospital gained the same relief, and in several cases it was noted that a visit to another house would cause wheezing.

One can theorize that in many of these babies the reagins in the bronchial mucosa are sufficient to produce symptoms, and at the same time the reagins in the skin are as yet insufficient to cause a positive scratch test.

CONCLUSIONS

These babies are, in general, sensitive to inhalants and foods. Although in many cases the attacks are precipitated by respiratory infections, it seems most likely that the babies with negative skin tests are also allergic to inhalants and foods, and that the respiratory infection is an additional factor.

122 Waterman Street

HUMAN VIRAL DISEASES

There are now listed twenty-seven human viral diseases, not including the eleven human rickettsial diseases. The latter are classified as pathogens intermediate in size and nature between bacteria and viruses. The viral diseases are grouped as follows: 7 dermatotropic, 8 neurotropic, 4 viscerotropic, 3 pantropic, 5 miscellaneous, such as influenza, common cold, epidemic keratoconjunctivitis, Newcastle disease virus conjunctivitis, and mumps. Allergy to viral infections has been reported. Allergists should consider the possibility of viral allergy when covering these diseases.

AIRBORNE FUNGUS SPORES, BRUNSWICK, GEORGIA, AREA

Incidence and Variation with Climatic Changes

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AIRBORNE mold spores have been established as important air contaminants which may incite inhalant allergies. Cadham's[2] first American report of a case of asthma due to fungi appeared in 1924, and the same year Van Leeuwen[26] reported in a British journal. The clinical importance of airborne molds is, as with the pollens, proportional to the concentration of the spores found in the atmosphere of a given community.[15] While seasonal, noninfective asthma is usually of pollen origin, it also may be due to spores of certain molds.[11,5] While molds exist throughout the entire year to some extent[5] the highest incidence may be seasonal like pollen counts. Therefore, the incidence of mold-sensitive patients may be seasonal.

Since his historical paper in 1934, Prince[21,22] has continued to draw attention to the importance of molds as frequent causes of respiratory allergic disease. Morrow, Prince, Lowe and Selle, since 1934, have continued to record instances showing the importance of these substances. These writers with other members of the Association of Allergists for Mycological Investigations have reports from various stations in eighteen states.[4,19,21,22] Kaplan's review[17] shows Durham[7,8,9,10] has given us data for some forty states.

Hansel[15] pointed out that the life cycle of Alternaria may be completed in two or three days, whereas the cycle for the ragweed pollen covers a period of five or six months. He stressed the difference in atmospheric changes on this short life cycle as compared to the effect on the pollen spores with the longer cycle. The importance of climatic conditions at the time of exposure is stressed also by Bruskin.[1]

Pratt[20] showed that the presence of airborne molds results in two types of reactions: (1) those which act as low grade bacteria and produce an infection of the lungs, body cavities and particularly the skin. (2) those which are entirely nonpathogenic, as certain molds, but act as sensitizers after the manner of the pollens and other airborne allergens.

Griffith[14] noted that in the Savannah area the warm periods during the winter months had no apparent effect on the abundance of molds as the corresponding temperature had during the summer.

It is therefore, desirable to study the incidence of molds from various sections of the country and if possible, these examinations should be interpreted as to the seasons, humidity and other atmospheric conditions. This is another report from the Southeastern section of the United States.

Presented at Eighth Annual Meeting, Southeastern Allergy Association, May 15-16, 1953, Nashville, Tennessee.

TABLE I. IDENTITY AND COUNT OF AIR BORNE MOLDS

	Jan. 23					Feb. 8					Feb. 21					March 6					March 30					April 15				
	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.
Acremonium	2				2																									
Alternaria	14		3		17		1			1	3	2	3		8	12	3		8	23	1	1	1		3	6	1			7
Aspergillus														2	2		1			1										
Botrytis																														
Cephalosporium			1		1																									
Cladosporium																						1			1					
Epicoccum			1		1	3				3							2			2										
Fusarium						1				1	2		1		3	9			5	14						1				1
Geolegnia			1		1							2			2															
Helminthosporium																														
Hormodendrum														3	3				4	4										
Monilia			5		5							1	2	1	4	4	5		6	15		2	4		6		2			2
Monosporium	10				10				1	1																				
Montospora				1	1																									
Mucor																														
Oospora			4	3	7	1				1		1			1		5	2	4	11			5		5			10		10
Paecilomyces																														
Penicillium		2			2	27		1	3	31			1	1	2	1				1	4		1	4	9	5	5	9	6	25
Phoma		1			1																1	1		2	4					
Pullularia		1		3	4		1			1		2			2															
Spondylacladium											3	1	2		6	15				15										
Sporotrichum	1				1																									
Stemphylium																														
Streptomyces																		1		1										
Torula		1			1																									
Trichoderma																														
Trichothecium																														
Sterile Hyphae		4	5	3	12	1	2			3	14	2	1	1	18	20				20	6			3	9				2	2
Unidentified						38			1	39	4	1			5	14		3		17								233		233
Total	27	9	20	10	66	71	4	1	5	81	26	12	10	8	56	75	16	6	27	124	12	5	11	9	37	12	8	252	8	280

TABLE I. IDENTITY AND COUNT OF AIR BORNE MOLDS—CONTINUED

	April 22					April 30					May 8					Sept. 11					Oct. 6					Oct. 24				
	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.
Acremonium																														
Alternaria	9	1	9	7	26	30	3	5	2	40		1	2		3	1				1	3	6			9		1			1
Aspergillus								3		3						7	12	4	3	26										
Botrytis																						1			1					
Cephalosporium							1			1																				
Cladosporium				1	1																									
Epicoccum																														
Fusarium			2	3	5			3	1	4	1			3	4															
Geolegnia			1		1							1			1															
Helminthosporium																					4				4					
Hormodendrum																														
Monilia			5		5																									
Monosporium																														
Montospora																														
Mucor																		4		4										
Oospora	5	1			6		1	6	2	9	7		1	13	21									5	5					
Paecilomyces																													1	1
Penicillium		3	3	3	9			7	2	9	1	1	1	7	10	2				2	8	2	45		55	9	1	9	1	20
Phoma																		3		3										
Pullularia			4		4			2		2																				
Spondylacladium																														
Sporotrichum																														
Stemphylium																3		1		4						1				1
Streptomyces																														
Torula																														
Trichoderma																						7			7					
Trichothecium																						2			2					
Sterile Hyphae								1		1	1	1		2	4	1		1		2										
Unidentified	31	10	31	6	78	36	1	10	1	48	9	2		9	20														1	1
Total	45	15	55	20	135	66	6	37	8	117	19	6	4	34	63	14	12	13	3	42	15	18	45	5	83	10	2	9	3	24

TABLE I. IDENTITY AND COUNT OF AIR BORNE MOLDS—CONCLUDED

	Oct. 30					Nov. 15					Dec. 14					Dec. 23					Total
	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	1	2	3	4	Tot.	
Acremonium																					2
Alternaria		1		1	2			1		1	1	2	2	3	8	3	3	6		12	162
Aspergillus	4			1	5						1		1	3	5				1	1	43
Botrytis																					1
Cephalosporium		7			7												2			2	11
Cladosporium								19		19	11	1	4		16						37
Epicoccum																					6
Fusarium			2		2																34
Geolegmia												3			3						8
Helminthosporium									1	1											5
Hormodendrum																					7
Monilia		1			1																38
Monosporium																					11
Montospora																					1
Mucor																					4
Oospora																			1	1	77
Paecilomyces																					1
Penicillium	4		1	7	12	20	15	4	8	47	6	5		2	13	6		2		8	256
Phoma																					8
Pullularia				2	2																30
Spondylacladium																					6
Sporotrichum																					1
Stemphylium	1		8	5	14	1		1		2	1				1						22
Streptomyces																					1
Torula																					1
Trichoderma																					7
Trichothecium			1		1																3
Sterile Hyphae			1		1									1	1						73
Unidentified																					441
Total	9	9	13	16	47	21	15	25	9	70	20	11	7	9	47	9	5	8	2	24	1296

Location I The marshes. ¾ horizon-miles of salt water marsh, ¼ marsh and scanty trees (palms and distant oaks).
Location II Downtown Business area—Outside ledge of second story office window. Very little flora.
Location III Residential Area—One block from marsh. Profuse flora, moss covered live oaks and hundreds of camellias and azaleas.
Location IV Residential Area—Sparse vegetation.

TABLE II. DISTRIBUTION OF TOTAL SPORES ISOLATED

Exposure Date	Location				Total
	1	2	3	4	
1-23-52	27	9	20	10	66
2- 8-52	71	4	1	5	81
2-21-52	26	12	10	8	56
3- 6-52	75	16	6	27	124
3-30-52	12	5	11	9	37
4-15-52	12	8	252	8	280
4-22-52	45	15	55	20	135
4-30-52	66	6	37	8	117
5- 8-52	19	6	4	34	63
9-11-52	14	12	13	3	42
10- 6-52	15	18	45	5	83
10-24-52	10	2	9	3	24
10-30-52	9	9	13	16	47
11-15-52	21	15	25	9	70
12-14-52	20	11	7	9	47
12-23-52	9	5	8	2	24
Total	451	153	516	176	1296

PROCEDURE

Plates on which these molds were isolated were potato dextrose agar adjusted to a pH of 3.5. This pH excluded obligate parasites such as rusts, smuts, and mildew which do not fruit in cultures,[1] and also inhibited bacteria. We used two petri plates for each exposure and they were exposed for seven and a half minutes. This procedure was adopted after earlier exposures of fifteen minutes had frequently resulted in more molds than the plates could accommodate. The plates were incubated at room temperature and the colonies examined and described from the fifth to the seventh day. They were then transplanted to Sabouraud agar slants and cover slip preparations made. A small amount of Sabouraud agar was placed on a slip and inoculated with a single colony, after which the slip was inverted on a slide, and three edges covered with paraffin. The slides with the cover slips were then placed in petri plates containing sterile moist filter paper. This method of preparation permitted examination of the specimens as they were growing without further transplatation or staining. Sterile technique was used throughout.[13,18,23,24,25,27,28]

Table I lists the 1,296 colonies isolated in this study. These comprise twenty-seven identified molds. There was a lapse of three months from the middle of May to September during which time we were unable to pursue this work because of laboratory personnel changes. However, the report includes sixteen dates well scattered throughout the remaining months with exposures made at four locations.

There were of course many colonies which did not produce fruiting structures. These were transferred to various preparations: potato dextrose agar, Sabouraud agar, cooked potatoes, brain-heart infusion, and we even tried to grow them on raw bananas. There were quite a number of colonies that we were unable to identify. Dr. Frederick A. Wolf of the Department of Botany, Duke University, Dr. Nathan Schaffer, of Orange, New Jersey, and Dr. Kenneth Raper, Peoria, Illinois, gave us invaluable assistance and helped with several of our identifications.

TABLE III. LOCATION COUNT MINUS OCCASIONAL FLOOD OF UNIDENTIFIED MOLDS

Exposure Date	Location				Total
	1	2	3	4	
1-23-52	27	9	20	7	63
2- 8-52	33	4	1	5	43
2-21-52	22	12	10	8	52
3- 6-52	55	16	6	27	104
3-30-52	12	5	11	9	37
4-15-52	12	8	19	8	47
4-22-52	14	15	24	14	67
4-30-52	30	6	27	7	70
5- 8-52	10	6	4	25	45
9-11-52	14	12	13	3	42
10- 6-52	15	18	45	5	83
10-24-52	10	2	9	3	24
10-30-52	9	9	13	16	47
11-15-52	21	15	25	9	70
12-14-52	20	11	7	9	47
12-23-52	9	5	8	2	24
Total	313 (451-138)	153	242 (516-274)	157 (176- 19)	865

Table I shows that on many occasions there were spore showers of unidentified molds, reaching the highest totals of 233 on April 15; seventy-eight on April 22; and forty-eight on April 30. These unknowns were chiefly of two types of colonies and they were among those that were sent to Drs. Wolf and Raper. Since the identification of molds present in a community in predominate quantities is of importance, it was considered proper to remove these unknown species from most of our calculations.

Table II shows the gross distribution of the total of the 1,296 colonies; however, in Table III the group of unidentified molds is subtracted from the totals giving counts that are apparently of more importance, since the colonies could be identified and probably represent the usual offenders for this community. Table III shows the distribution of 865 mold colonies which were identified and upon which most of the graphs and subsequent analyses are based. It is noted that locations 1 and 3 yield the highest counts in these charts. Location 1 is on the marsh, and location 3 is only one block from the marsh; location 3 is the site where there are the greatest number of trees, flowers, and other vegetation.

From January through April, 1952, we were making exposures both indoors and outdoors. Wallace, Weaver and Scherago[27] included indoor locations in their reports. In 1950, Christensen[3] showed that mold spores liberated on the first floor of a four-story building were found throughout the entire building within a relatively few minutes. To further show such dissemination, in April we made a count with one plate placed on a divan on which a man sat down several times. Simultaneously, we exposed another plate elsewhere in the room. We discovered that the plate exposed on the divan grew eighteen colonies of ten different types whereas the other plate contained only one colony. In other words, a person coming into the room and sitting down would in this case have

TABLE IV. COUNTS MADE INSIDE AND OUTSIDE BEFORE THIS COMPARATIVE STUDY WAS DISCONTINUED

Exposure Date	Location Inside			Location Outside		
	1	2	3	1	2	3
1-23-52	7	2	1	20	10	9
2- 8-52	4	1	—	1	5	4
2-21-52	5	6	3	10	8	12
3- 6-52	4	—	—	6	27	16
3-30-52	7	3	—	11	9	5
4-15-52	13	12	4	41	8	8
4-22-52	16	9	3	64	20	15
Total	56	33	11	153	87	69

TABLE V. DOMINANT MOLDS. EACH DATE—EACH EXPOSURE

Location	Penicillium	Alternaria	Monilia	Cladosporium	Aspergillus	Pullularia	Oospora	Spondylacladium	
I	2- 8 3-30 5- 8 10- 6 10-24 10-30 11-15 12-23	1-23 4-15 4-22 4-30		12-14	9-11 10-30	3- 6		2-21	
II	1-23 4-15 4-22 5- 8 11-15 12-14	2- 8 2-21 4-30 5- 8 12-23	3- 6	11-15		2- 8 2-21	3- 6 3-30		Phoma 1-23
III	2- 8 4-15 4-30 10- 6 10-24	2-21 5- 8 12-23	1-23 2-21 4-22	11-15 12-14	9-11		3- 6 3-30	2-21	Mucor 9-11 Stemphylium 10- 7
IV	2- 8 3-30 4-15 4-30 10-24 10-30 11-15	4-22 4-30 12-14	3- 6		9-11 10-30 12-14 12-23	1-23	1-23 5- 8 10- 6 12-23		Torula 2-21

Penicillium 26 Alternaria 15 Aspergillus 7 Oospora 8 Monilia 5.

been exposed to eighteen times the concentration of molds as would be indicated by an atmospheric count of the same room. Such molds agitated by the bellows action of the cushions and disseminated into the air are probably part of the housedust mold population.[5] With this information and viewpoint, we considered the exposures made indoors of little importance and they were discontinued. In line with other reports, our indoor and outdoor exposures up to that time, however, showed a preponderance of three to one of the outside air over the inside air. The comparison of indoor and outdoor exposures is given in Table IV. The molds obtained on these indoor exposures are not included in the report elsewhere.

Morrow, Lowe and Prince[19] stated that aspergillus and penicillium are dominant so many times that they may be considered cosmopolites. In Table V we show the occurrence of the dominant molds on each

date. Should two or more molds have been present in equal number each mold is entered as dominant. This table shows that penicillium was a dominant twenty-six times, alternaria fifteen, oospora eight, aspergillus seven, and monilia five times.

The grand total column of Table I shows that the dominant molds in frequency were also dominant in the number of colonies. This table shows 256 colonies for penicillium, 162 for alternaria, and seventy-six for oospora, with lower counts for other molds. This relationship holds throughout most of the charts showing that the dominant identified molds retained their relative frequency not by sudden showers of spores, but also by appearances in large numbers.

Figure 1 shows graphically the incidence of the identified molds throughout the different seasons. Here, our one highest count was made early in March, and in general, the first few months of the year showed the greatest number of molds. Similar graphs of the same Figure show the occurrence of each individual mold. Penicillium is present throughout the entire year with its highest peak in the fall, whereas alternaria is also present throughout the entire year with its peak in the first few months of the year. Aspergillus showed a single high peak in September with low counts occurring irregularly in other months. Oospora and monilia each occurred almost exclusively in the spring.

Figure 2 shows the temperature variation, wind velocity and total mold counts. In considering the wind and temperature effect, the gross mold count was again used whereas the previous graphs were of identified molds. A study of the gross mold occurrence shows very little correlation between the temperature curve and the height of the graphs. The spring and early summer showed higher temperatures, but the mold populations did not parallel the temperature curve; while higher counts were observed, the impression is that the mold fluctuation represents a general seasonal variation and is not merely proportional to the temperature variation.

The wind velocity is shown as a mean morning velocity (a broken single line); and as a mean afternoon velocity (a double dotted line). All of our exposures were made in the afternoon. Perhaps this accounts for the fact that in February the highest wind velocity did not yield the highest count; but when we had the incursion of the unidentified molds, there was a very high morning and also a high afternoon wind. This, we think, explains the presence of these unidentified molds that were found on those dates. The importance of wind velocity makes itself evident again in the study of the Fall graphs of relative humidity. On November 15, Figure 3, there was an extremely high humidity, the highest recorded in the year; we would expect a high count, but on this date there was during the morning an average wind velocity of two knots per hour and during the afternoon when the exposures were made there was a zero velocity. The most humid day was on September 11, when

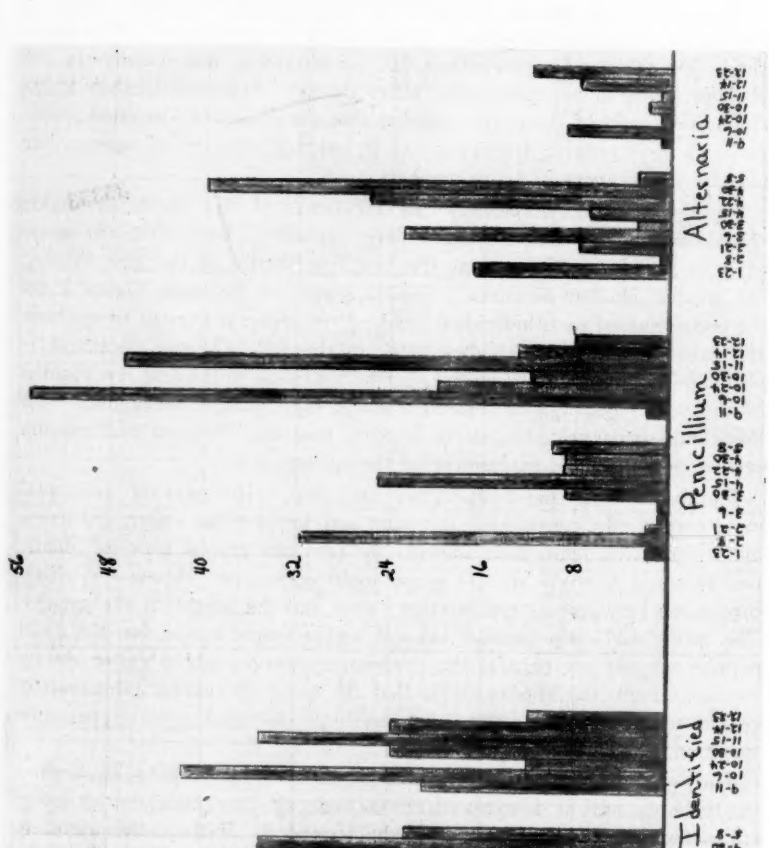
112
96
80
64
48
32
16
0
56
48
40
32
24
16
8
Total Identified
Penicillium
Alternaria

Fig. 1a.

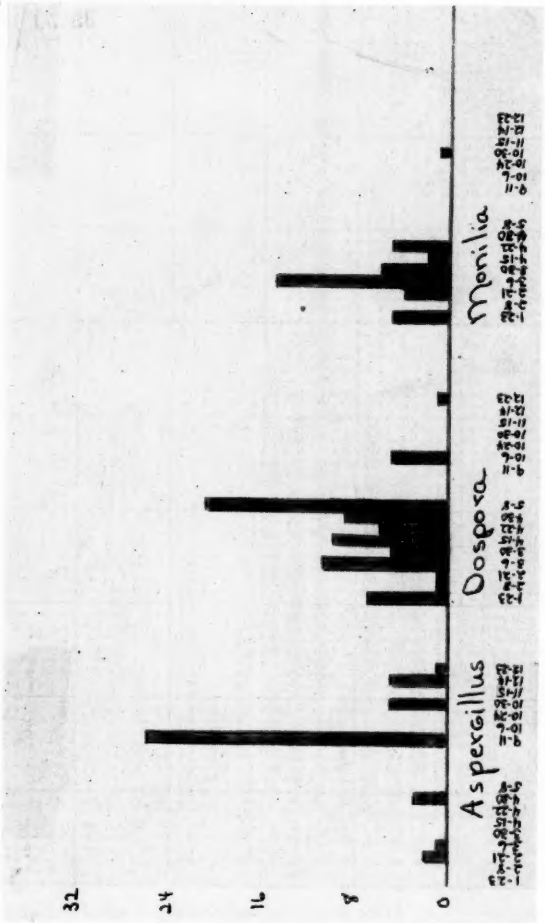

Fig. 1b.

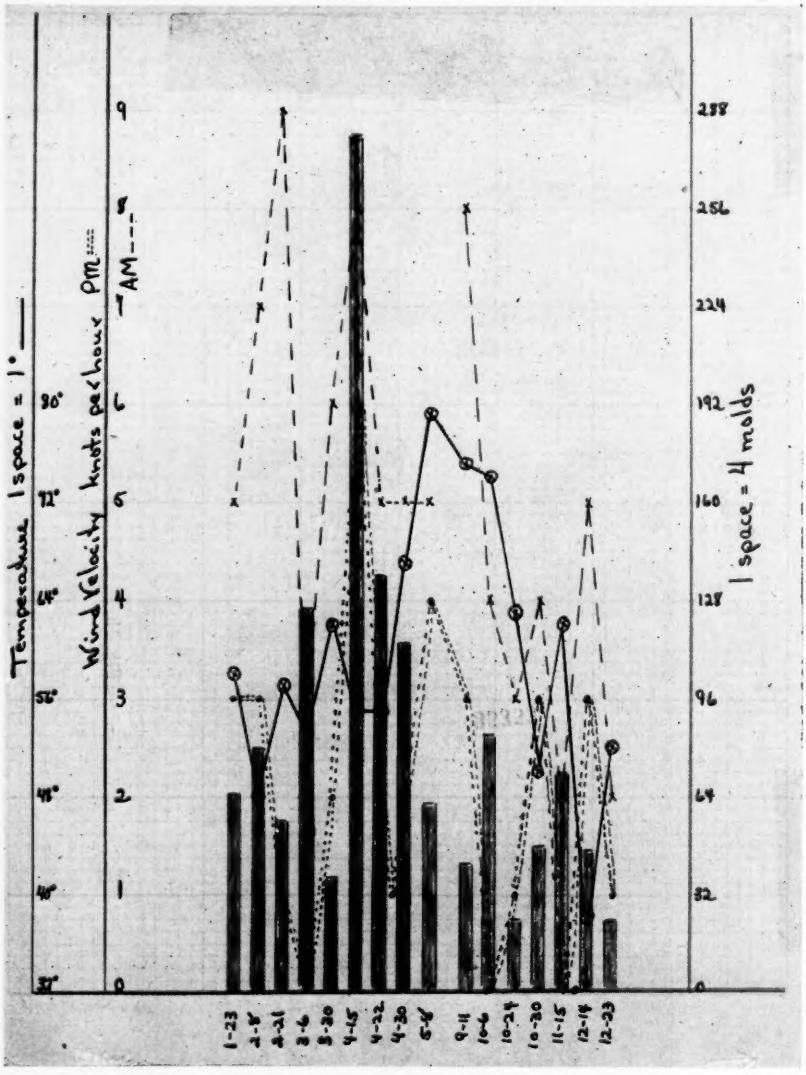

Fig. 2. Gross Mold Count; temperature and wind velocity.

during the morning, there was a fair wind; however, during the afternoon when the exposure was made the wind velocity averaged only three knots per hour. In the extremely humid days in December (humidity 70 per cent) there was a low wind velocity of three and one knots per hour. From these two graphs, it seems that the most important climatic

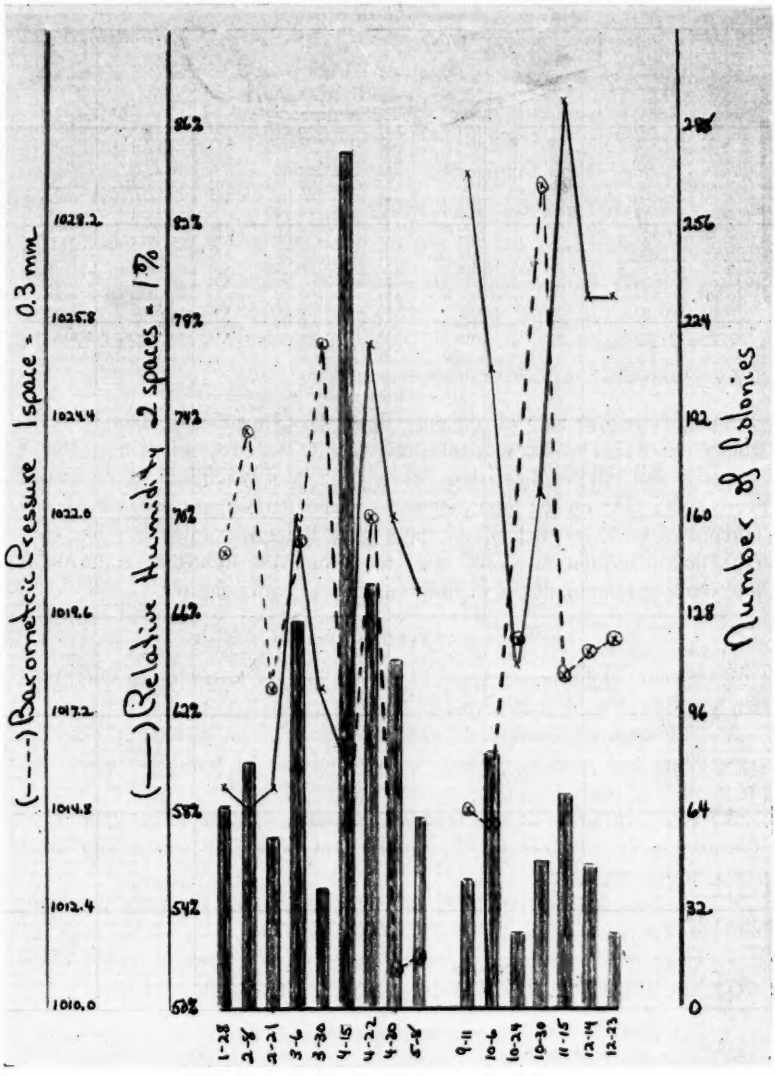

Fig. 3. Total Mold Count; barometric pressure and relative humidity.

factor is the velocity of the wind when the exposures are made. I was unable to determine any relationship between the direction of the wind at the time of each exposure and the occurrence of the molds. The direction of the wind at the time of each exposure is recorded in Table VI.

TABLE VI*

Date 1952	Mean Relative Humidity	Mean Temperature	Mean Pressure	Average Wind Direction	Average Wind Velocity Knots p. h.	Total Precipitation
1-23	59%	58 F	1021.3	AM N —PM NE	AM 5—PM 3	.10
2- 8	58	48	1024.0	AM NW—PM SW	AM 7—PM 3	None
2-21	59	57	1017.9	AM NW—PM NW	AM 9—PM 1	None
3- 6	70	53	1021.4	AM E —PM E	AM 3—PM 0	None
3-30	63	62	1025.2	AM NE —PM NE	AM 5—PM 2	None
4-15	60	55	1014.4	AM W —PM W	AM 8—PM 6	None
4-22	77	55	1022.1	AM SE —PM SE	AM 5—PM 2	None
4-30	70	67	1010.8	AM N —PM N	AM 5—PM 1	None
5- 8	67	79	1011.4	AM W —PM W	AM 5—PM 4	.02
9-11	84	75	1014.9	AM SE —PM S	AM 8—PM 3	.06
10- 6	76	74	1014.6	AM E —PM NE	AM 4—PM 0	None
10-24	64	63	1019.1	AM E —PM E	AM 3—PM 1	None
10-30	71	50	1029.1	AM N —PM N	AM 4—PM 3	None
11-15	87	62	1018.2	AM N —PM N	AM 2—PM 0	None
12-14	79	38	1018.8	AM N —PM W	AM 5—PM 3	Trace
12-23	79	52	1019.2	AM E —PM S	AM 2—PM 1	None

*Meteorological office. U. S. Naval Air Station. Glynco, Georgia.

Since there was rainfall on only three days, insufficient data is available from which to draw conclusions relative to effect of rains. But it is noted that on the three days when there was precipitation the counts were lower than on the next exposures even though there was a moderate amount of wind on each of the days when there was rainfall. The concept that precipitation would tend to cleanse the atmosphere of molds and other contaminants is in line with these scanty figures.

CONCLUSIONS

1. Twenty-eight molds were identified in this area during this 1952 study. There were 1,296 colonies isolated.

2. The dominant identified molds were penicillium, alternaria, oospora, aspergillus and monilia. These were dominant in both frequency and in number of colonies.

3. Wind variation at the time of exposure was the most striking of the atmospheric factors on the mold count. Rainfall seems to cleanse the atmosphere.

4. The seasonal variation of the total count and for each dominant mold is shown.

5. High winds produced a sudden influx of two types of molds which were not identified. These were present in high concentrations.

BIBLIOGRAPHY

1. Bruskin, Syril: A comprehensive survey of the incidence of fungus spores in the New Brunswick, New Jersey, area. Ann. Allergy, 11:1, 1953.
2. Cadham, F. T.: Asthma due to grain rusts. J.A.M.A., 83:27, 1924.
3. Christensen, Clyde M.: Intramural dissemination of spores of hormodendrum resinae. J. Allergy, 21:409, 1950.
4. Committee of Allergists for the study of unknown causes of hay fever and asthma: Molds and their relation to allergy. Ann. Allergy, 1:54-59, 1943.
5. Cook, Robert A.: Allergy in theory and practice. Philadelphia: W. B. Saunders & Company, 1947.
6. Criep, Leo H., and Hammond, M. L.: Regional factors in allergy. Ann. Allergy, 10:282-287, 1952.

7. Durham, O. C.: Incidence of airborne fungus spores I alternaria. J. Allergy, 10:480-490, 1937.
8. Durham, O. C.: Incidence of airborne fungus spores II alternaria, Hormodendrum and rusts. J. Allergy, 10:40-49, 1938.
9. Durham, O. C.: Atmospheric molds in Alaska. J. Allergy, 12:307-309, 1941.
10. Durham, O. C.: The volumetric incidence of atmospheric allergies. J. Allergy, 18:231-238, 1947.
11. Feinberg, Samuel M.: Seasonal hay fever and asthma due to molds. J.A.M.A., 107:1861-1867, 1936.
12. Feinberg, Samuel M.: Mold allergy, its importance in asthma and hay fever. Wisconsin M. J., 34:254, 1935.
13. Gilman, Joseph C.: A Manual of Soil Fungi. The Iowa State College Press, 1950.
14. Griffith, B. T.: Mycological studies in the Savannah area—1950. J. Allergy, 22:461-465, 1951.
15. Hansel, French K.: Hay fever. J. Missouri M. A., 37:241-246, 1940.
16. Hopkins, J. G.; Benham, R. W., and Kesten, B. M.: Asthma due to the fungus alternaria. J.A.M.A., 94:6-10, 1930.
17. Kaplan, Leo H.: Survey of airborne fungus spores of the Boston area in relation to inhalant allergies. Ann. Allergy, 10:109, 1952.
18. Lewis, George M., and Hopper, Mary E.: An Introduction to Medical Mycology. Chicago: Yearbook Publishing Co., 1948.
19. Morrow, Marie B.; Lowe, E. P., and Prince, Homer E.: Mold fungi in the etiology of respiratory allergic diseases. J. Allergy, 13:215-226, 1942.
20. Pratt, Henry N.: Seasonal aspects of asthma and hay fever in New England. New England J. Med., 219:782-786, 1938.
21. Prince, Homer E., and Morrow, Marie B.: Molds in the etiology of asthma and hay fever with special reference to the coastal areas of Texas. South. M. J., 30:754-762, 1937.
22. Prince, Homer E.; Selle, W. A., and Morrow, Marie B.: Molds in the etiology of asthma and hay fever. Texas State J. Med., 30:340-343, 1934.
23. Raper, Kenneth B., and Thom, Charles: A Manual of the Penicillia. Baltimore: William and Wilkins Company, 1949.
24. Smith, George: An Introduction to Industrial Mycology. London: Edward Arnold Company, 1947.
25. Thom, Charles, and Raper, Kenneth B.: A Manual of the Aspergillus. Baltimore: Williams and Wilkins Company, 1945.
26. Van Leeuwen, W. S.: Bronchial asthma in relation to climate. Proc. Roy. Soc. Med., 17:19-22, 1924.
27. Wallace, Elizabeth M.; Weaver, R. H., and Scherago, M.: A weekly survey of molds and dust in Kentucky. Ann. Allergy, 8:202, 1950.
28. Wolf, Frederick A., and Wolf, Frederick T.: The Fungi (two volumes). New York: John Wiley and Sons, 1947.

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SILICONE CREAM IN INDUSTRY

Dr. Raymond R. Suskind of the University of Cincinnati College of Medicine at the recent meeting of the American Medical Association in New York announced good results with silicone cream to protect the skin of industrial workers. It is now used extensively in industry and the one incorporated in a cream is polymethyl siloxane. The cream consists of 52.5 per cent silicone fluid mixed with inert clay, bentonite. It is a thin, inconspicuous film which can be spread on the skin when commencing work and easily removed at the end of the day. Seven months' continuous use of this silicone cream caused no harmful effects in any way.

THE USE OF TRYPTAR (TRYPSIN) IN BRONCHIAL ASTHMA AND OTHER RESPIRATORY CONDITIONS

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IN A RECENT publication[10] we pointed out how we became interested in efforts to loosen or dissolve the thick tenacious materials which interfere with the breathing of patients with bronchial asthma and other respiratory conditions. In 1937, because of marked local reactions with hemoptysis and hoarseness in animals and humans, we were forced to stop inhalations of an enzyme made from the fruit of Carica papaya. Now, and since early in 1952, we are using inhalations of trypsin (Tryptar®),* an enzyme found in the body, which digests necrotic tissue without adverse action on living tissues. "This enzyme has a broad spectrum of vigorous proteolytic action on protein, denatured protein, true peptones, respiratory and intestinal mucin, fibrin and protein split products. The final degradation products of tryptic digestion are small polypeptides and some amino acids. Tryptar® does not digest living tissue since both serum and viable cells contain specific trypsin inhibitors as well as nonspecific inhibitory substances which act as protective mechanisms against proteolytic digestion. This selectivity of digestion plus the absence of antigenicity or sensitivity appeared to us, as well as to a number of other workers, as a preparation well worth investigation."[10]

Our cases were studied both in Wesley Memorial Hospital and in our office, and, as the tables show, a variety of respiratory conditions were treated with the inhalations. Among these were patients with (1) bronchial asthma, acute and chronic, and with or without infectious complications; (2) bronchiectasis, alone or mixed with asthma; and (3) acute atelectasis.

Our results are shown in Tables I through VII, and deserve some critical analysis. It is obvious from our findings and those of others that "Tryptar aerosol constitutes an ideal agent for removing from the respiratory track thick sputum which the patient is unable to expel. Generally speaking, the thicker the sputum and the greater the volume, the better are the results."[10]

We had hoped that this aerosol would be the answer for patients with bronchial asthma, with or without emphysema. We know that thick sputum, often to the point of dessication, is present in our most severe

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*Tryptar was supplied through the courtesy of the Armour Laboratories, Chicago, Illinois.

Presented at the Ninth Annual Congress of the American College of Allergists, April 27, 1953, Chicago, Illinois.

TABLE I. TRYPTAR® AEROSOL IN PAROXYSMAL BRONCHIAL ASTHMA

Name	Age	Sex	No. Treatments	Total Dose (Units)	Results	Remarks
1. T.D.	9	M	2	150,000	Good	Wheezing and dyspnea lessened.
2. P.B.	36	F	2	250,000	None	
3. M.G.	29	M	1	250,000	Excellent	Chest cleared rapidly.
4. E.S.	41	F	2	250,000	Excellent	Also received ACTH and epinephrine.
5. G.W.	11	F	8	1,000,000	None	
6. M.W.	44	F	4	1,000,000	Excellent	Transient rash, upper lip.
7. M.W.	44	F	4	500,000	Excellent	Second admission of Case No. 6. No rash this time.
8. E.D.	36	F	4	500,000	Good	Some basal rales.

cases—this has been repeatedly shown at autopsies done in the relatively occasional patient who succumbs during an attack. Unfortunately, as shown in Table II, the results in chronic bronchial asthma with emphysema were not too good. Excellent relief occurred in only five of thirty-three cases, with good results in another ten, and no apparent help in the other eighteen. We had not, of course, expected that any enzyme could possibly alter the structural deformities present in emphysema, but we thought that the Tryptar® would be most useful in liquefying and removing the thick mucus plugs which are commonly present in these chronic asthmatic individuals.

The results in paroxysmal bronchial asthma were much better (Table I). Excellent relief occurred after inhalations in four of eight patients, with good results in two of the other four. Here, obviously, the sputum is not as sticky and gelatinous as in the chronic asthmatic.

As shown in Table III, we obtained excellent results in ten of fourteen patients whose bronchial asthma was complicated by some type of infectious bronchitis or pneumonitis. Rales, fever and x-ray findings disappeared rapidly in the successful cases, even in a few patients who had not been helped by antibiotics.

There were twenty-one patients with bronchiectasis (Table IV), and in fourteen of these, excellent relief followed after two to eleven inhalations, with total dosages varying from 200,000 to 1,750,000 units. In some patients the sputum collected again after the aerosol had been stopped, and further inhalations also gave good to excellent results.

In the five patients with acute atelectasis (Table V), we obtained excellent results in four. In the first patient, unfortunately, bronchoscopic aspiration was done just before the Tryptar® became available. Nevertheless, rales remained after the bronchoscopic aspiration, and these disappeared following inhalations of the enzyme. In some patients the inhalation seems to cause tickling of the throat with resultant cough and expectoration, even in surgically treated patients who had refused to cough because of postoperative pain. It would seem, therefore, that in acute or impending atelectasis, inhalations of Tryptar® might well be tried first before resorting to bronchoscopic aspirations.

TABLE II. TRYPTAR® AEROSOL IN CHRONIC BRONCHIAL ASTHMA

Name	Age	Sex	No. Treatments	Total Dose (Units)	Results	Remarks
1. I.B.	56	F	3	275,000	None	Hoarseness after first and third treatments; much sputum. Treatment stopped because of hoarseness.
2. M.B.	21	F	6	700,000	None	Sputum increased after first two inhalations, but asthma continued.
3. C.C.	63	M	4	500,000	None	Cardiac factor?
4. M.H.	37	M	6	750,000	None	Asthma continues.
5. I.M.	52	F	6	750,000	Good	Some expectoration; neurotic factor.
6. M.R.	70	F	2	250,000	None	Hoarse after second treatment, lasted ten days.
7. L.S.	75	M	4	475,000	Excellent	Coughed up three basins full of thick, purulent sputum.
8. H.S.	55	M	1	125,000	Good	Neurotic element.
9. E.T.	70	M	4	500,000	Good	
10. W.T.	66	M	4	500,000	Good	
11. I.W.	75	F	3	250,000	Good	Hoarseness and wheezing after first treatment. Much sputum expectorated.
12. J.W.	59	F	5	625,000	None	Neurosis three plus; difficult to evaluate.
13. T.B.	72	M	4	500,000	Excellent	Much thick, grey-green sputum expectorated.
14. J.B.	57	F	3	375,000	None	Associated with pulmonary tuberculosis, hoarseness, and positive sputum.
15. J.F.	20	M	4	1,000,000	None	Much sputum and plugs expectorated but asthma continued.
16. J.G.	41	F	2	250,000	None	Hoarseness after second inhalation; very neurotic.
17. W.M.	47	M	4	875,000	Good	
18. A.P.	76	F	2	250,000	None	
19. R.S.	34	M	4	1,625,000	None	
20. R.E.	74	M	2	250,000	None	Emphysema two plus.
21. J.R.	64	M	6	750,000	Good	Asthma after two of six treatments. Severe emphysema.
22. S.M.	64	F	3	300,000	None	Mild hoarseness after first inhalation.
23. C.B.	51	M	1	125,000	None	Dyspnea increased. Claustrophobia.
24. G.H.	50	M	5	575,000	None	Asthma after first treatment only. Very severe emphysema.
25. W.V.	56	M	4	500,000	Excellent	
26. L.W.	63	F	4	500,000	Excellent	
27. C.P.	64	F	4	500,000	Excellent	Very productive coughing after each treatment.
28. W.V.B.	61	M	4	500,000	Good	
29. B.T.	54	F	6	650,000	Good	Much sputum.
30. A.O.	63	M	3	325,000	None	
31. C.M.	49	F	1	125,000	None	Hoarse and increased dyspnea; inhalations stopped.
32. T.C.	57	M	3	275,000	Good	Coughed up great deal sputum.
33. J.D.	28	M	5	525,000	None	Positive sputum first obtained after inhalations. (Was suspect T.B. for years). Now in sanitarium.

DISCUSSION

As shown in these tables dealing with eighty-one patients, excellent results followed in thirty-seven cases, good in twenty-two, with failures in twenty-one. The most benefit was obtained in patients with thick or copious sputum as in bronchiectasis, acute atelectasis, and pulmonary infections of various types. In paroxysmal asthma, relief occurred in six of eight patients. Our poorest results, unfortunately, were in those who most sorely need relief, i.e., the patient with chronic asthma and emphysema. We cannot expect to clear emphysema, but we should be able to help the patient rid himself of the sticky material which obstructs his air passages. It may well be that our relatively poor results in these patients has been due to the possibility, or even probability, that the enzyme was not able to descend far enough down the bronchial tree and thus could not liquefy the tenacious secretions. If this is true, then it follows that the inhalations must be preceded by more potent bronchodilators. Before inhalations we have been injecting subcutaneously 0.25 cc 1:1,000 epinephrine and 0.75

TABLE III. TRYPTAR® AEROSOL IN BRONCHIAL ASTHMA WITH INFECTIOUS BRONCHITIS AND PNEUMONITIS

Name	Age	Sex	No. Treatments	Total Dose (Units)	Results	Remarks
1. R.F.	50	M	5	600,000	Good	Tightness and asthma after first treatment only. Good relief, but not complete.
2. G.H.	11	F	4	375,000	Excellent	Mild hoarseness after second treatment, rales in LLL disappeared after third treatment.
3. R.J.	57	M	5	625,000	Excellent	Rhonchi disappeared, but still an occasional wheeze.
4. M.H.	36	F	3	375,000	Good	Hoarseness after second treatment; removal of much tenacious sputum. Also receives inhalations streptomycin.
5. B.S.	34	F	4	1,000,000	Excellent	Hoarseness and coughing after each treatment; dosage probably too large.
6. H.W.	51	M	3	375,000	Good	Occasional wheeze persists.
7. A.P.	42	F	3	375,000	Good	Patient felt much better.
8. I.C.	47	F	4	625,000	Excellent	Low grade fever of three weeks disappeared after first treatment.
9. E.D.	36	F	4	500,000	Excellent	Fever and rales disappeared.
10. B.S.	15	F	4	425,000	Excellent	Fever and rales disappeared.
11. N.E.	56	M	4	1,000,000	Excellent	Hoarseness after first inhalation only. Vital capacity increased from 33 to 90 per cent; chest cleared completely. Also had penicillin.
12. M.C.	33	F	3	275,000	Excellent	Much sputum after second inhalation.
13. H.C.	60	M	4	425,000	Excellent	Coughed up much sputum.
14. J.F.	5	M	4	200,000	Excellent	Much sputum after each of first three inhalations.

cc Histadyl® or Benadryl.® Perhaps this mixture is not sufficient. We will substitute intravenous aminophylline in some cases, and inhalations of 1:100 epinephrine or 1:200 Isuprel® in others, and we can only hope for a larger percentage of success in this group.

Inhalations of Tryptar® do not, of course, constitute a cure; when they are successful the relief may be temporary and further inhalations may be necessary. But they give excellent results in most patients with thick or copious sputum, and as one physician remarked, they act as an excellent "garbage remover."

UNTOWARD REACTIONS

Transient hoarseness occurred after seventeen of the 312 inhalations given to these eighty-one patients. However, at first we gave larger doses, as much as 250,000 units, and probably gave it too rapidly. We learned to give the inhalations more slowly and to use smaller doses, and now each patient is instructed to wash out his mouth with water after each inhalation. Hoarseness still occurs, but much less often and much less severe. In some individuals additional inhalations were given with no recurrence of hoarseness. In five patients there was an increase of dyspnea and wheezing after inhalations, but psychic factors may be as important here as the enzyme itself. The mask over the nose and mouth seems to be feared by a few patients. One of the medical technologists who administers the aerosolizations develops some temporary burning of the eyes and rawness of the throat.

PREVIOUS CLINICAL WORK

As mentioned in our previous publication,[10] "The first clinical paper

TABLE IV. TRYPTAR® AEROSOL IN BRONCHIECTASIS WITH OR WITHOUT BRONCHIAL ASTHMA

Name	Age	Sex	No. Treatments	Total Dose (Units)	Results	Remarks
1. W.A.	78	M	4	500,000	Excellent	Coughed up 120 cc thick sputum within one hour after fourth treatment. Patient working daily for first time in three months.
2. I.C.	45	F	11	1,375,000	Excellent	After first treatment expectorated 120 cc of tenacious yellow-green sputum with many plugs. Has had three series of inhalations, all with excellent results.
3. I.D.	37	F	3	275,000	Good	Severe hoarseness with first treatment only.
4. P.F.	19	M	2	500,000	Excellent	Coughed up very thick sputum. Patient did not return.
5. R.G.	67	M	2	500,000	Excellent	Patient felt he had recovered; remains much improved.
6. W.K.	62	M	8	2,000,000	Excellent	Excellent results after first four treatments; returned to work. Received second course six weeks later with equally good results.
7. J.P.	47	M	2	500,000	Excellent	Patient refused more as he felt he was "cured." Did not return.
8. T.P.	63	M	4	500,000	Excellent	Chest cleared. No follow-up.
9. M.M.	58	M	2	200,000	Good	Coughed up much thick sputum, but had nausea and vomiting and dyspnea. No trouble from second inhalation, but refused further treatment.
10. J.R.	66	M	3	275,000	Excellent	Much expectoration of thick sputum, with hoarseness after first inhalation. Also has congenital heart disease.
11. A.S.	36	F	4	450,000	Excellent	Much expectoration; low grade fever of three weeks disappeared after second treatment. Hoarse for three days after last treatment.
12. W.D.	45	M	8	1,750,000	Excellent	Old tuberculosis and severe bronchiectasis for fifteen years. Patient had two courses and requests treatment every sixty days.
13. A.G.	62	M	2	250,000	Good	Apparently had good result but did not return for treatment.
14. R.A.	54	M	4	500,000	Excellent	Patient reported excellent results, although sputum not excessive after inhalations.
15. A.B.	60	F	6	475,000	Excellent	Much thick sputum expectorated; diminution of bubbling rales; feels better. Severe hemoptysis occurred two months after inhalations were stopped.
16. D.L.	57	M	5	575,000	Good	Rales fewer after inhalations.
17. W.K.	49	M	6	700,000	Excellent	Marked kyphoscoliosis and bronchiectasis. Much expectoration at first, less later; rales fewer.
18. J.D.	45	M	5	550,000	None	Old empyema scar. Treatment stopped. Also on streptomycin inhalation.
19. M.D.	60	F	6	650,000	Excellent	Cylindrical bronchiectasis. All rales disappeared; patient working.
20. R.B.	26	F	6	525,000	Good	Saccular and cylindrical bronchiectasis (severe). Associated with marked kyphoscoliosis and dwarfism.
21. R.G.	36	M	4	425,000	Fair	Mild asthma after last inhalation.

presented on Tryptar® pertained to the significant value of its intrapleural administration in the sterilization and re-expansion of selected tuberculous and nontuberculous fibrino-purulent empyema cases.[5] This was followed shortly by articles[1,2,4,6,8] on the use of the enzyme in the local therapy of many suppurative and necrotic lesions, such as grossly contaminated amputation stumps, subcutaneous hematomas, chronic osteomyelitis, diabetic gangrene, slough wounds after failure of skin grafts, and decubitus and varicose ulcers. The use of Tryptar® by inhalation was commented on by Unger,[9] Roettig et al,[7] and Limber et al;[3] the latter reported on studies undertaken in patients with active pulmonary tuberculosis who had tenacious sputum, as well as in patients who had other conditions in which the high viscosity of the sputum presented a problem.

Limber and his co-authors stated[3] that "*In vitro,* 50,000 units of crystal-

TABLE V. TRYPTAR® AEROSOL IN ATELECTASIS

Name	Age	Sex	No. Treatments	Total Dose (Units)	Results	Remarks
1. S.S.	34	F	4	500,000	Excellent	Preceded by aspiration bronchoscopy; rales after bronchoscopy disappeared following trypsin inhalations. Well past nine months.
2. R.S.	26	M	1	250,000	Excellent	LLL atelectasis (after gastroenterostomy) cleared quickly; coughed up 180 cc of thick sputum and vomitus. In four hours T.P.R. changed from 102.4 F., 124, 36, to 100.2 F., 96, 24.
3. T.S.	51	M	1	500,000	Excellent	After gastric resection refused to cough. Tryptar® given in 7 cc of diluent over one-half hour. Removal of much sputum and plugs; re-expansion of LLL three hours later (x-rays).
4. W.R.	72	M	4	1,000,000	Excellent	Post-op esophageal resection followed by probable atelectasis; cleared nicely.
5. T.R.	67	M	2	500,000	Good (for a time)	Gastric resection. Inhalations started four days postoperative while moribund. Much sputum obtained, but died fourteen hours after first inhalation. Autopsy denied.

TABLE VI. RESULTS OBTAINED WITH TRYPTAR® AEROSOL IN EIGHTY-ONE CASES (312 INHALATIONS)

Diagnosis	No. Cases	Results			
		Excellent	Good	Fair	None
Paroxysmal Bronchial Asthma	8	4	2		2
Chronic Bronchial Asthma with Emphysema	33	5	10		18
Bronchial Asthma with Infectious Bronchitis or Pneumonitis	14	10	4		
Bronchiectasis, with or without Bronchial Asthma	21	14	5	1	1
Atelectasis (Acute)	5	4	1		
Total	81	37	22	1	21

line trypsin produces a dramatically rapid liquefication in 25 cc samples of thick sputum obtained from patients with active pulmonary tuberculosis." This lysis was reflected by a decline in the measured sputum viscosity. Rabbits were also subjected to trypsin aerosolization, and showed no marked histologic deviation from the normal appearance of the tracheobronchial tree and lung parenchyma. These authors concluded that "aerosol trypsin is relatively nontoxic, harmless to respiratory tissue, and does not impede ciliary action."

ADMINISTRATION

Dosages.—We began this study with dosages of 125,000 to 250,000 units of Tryptar® aerosol, but hoarseness followed too frequently in these early cases, and now we usually begin with 75,000 units dissolved in 1.5 cc of the diluent (Sorensen's Phosphate Buffer Solution.) If no reaction follows, we increase to 100,000 units in 2 cc of the diluent, and later to 125,000 in 2.5 to 3 cc (top dose.)

Technique.—As mentioned in our previous publication,[10] we begin by injecting 0.25 cc 1:1,000 epinephrine and 0.75 cc of a soluble antihistamine, e.g., Histadyl® or Benadryl,® to dilate the bronchial tree and perhaps to lessen hoarseness and dyspnea.

TABLE VII. UNTOWARD REACTIONS OBSERVED WITH 312 TRYPTAR® AEROSOLIZATIONS IN EIGHTY-ONE PATIENTS

Hoarseness, Transient	17
Increased Asthma	5
Rash About Lips	1
Nausea and Vomiting	1
Total Reactions	24

The "mask method" of aerosolization is used, which consists of rubber tubing extending from the oxygen tank to a Vaponefrin plastic nebulizer. The nebulizer is attached directly to a BLB mask rebreathing bag apparatus. After placing Tryptar® aerosol in the nebulizer, the mask is strapped to the face with crevices being closed with cotton or moist gauze to prevent escape of the enzyme, and moist gauze dressings are placed over the patient's eyes. Usually ten to fifteen minutes are required to nebulize 1.5 to 2.0 cc of Tryptar® solution when using a flow rate of four to six liters of oxygen per minute.

In order to avoid nasal or oral irritation, patients are advised to inhale through the mouth and exhale through the nose during aerosolizations and, immediately upon discontinuation of the treatment, to blow the nose and wash out the mouth with water, and then to drink a glass of water.

SUMMARY AND CONCLUSIONS

1. Tryptar® (trypsin) was used 312 times by aerosol in eighty-one patients with bronchial asthma and other respiratory conditions. This enzyme, which is nontoxic and does not appreciably affect living tissues, lessens the viscosity of materials which collect in the bronchial tree.

2. Inhalations are very effective in removing thick sputum which the patient is unable to expectorate.

3. In chronic bronchial asthma with emphysema the results were disappointing, with excellent relief in only five of thirty-three cases, with improvement in another ten, and failure in eighteen.

4. Much better relief occurred in our few patients with paroxysmal bronchial asthma, and spectacularly excellent results occurred after inhalations given to patients with bronchial asthma plus some pulmonary infectious process, and in those with bronchiectasis.

5. In atelectasis Tryptar® inhalations work so well that the procedure should be tried first before resorting to bronchoscopic aspirations.

6. Tryptar® aerosol is a safe procedure, and hoarseness, the only troublesome side effect, is infrequent and mild if care is used.

ACKNOWLEDGMENT

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Catherine H. Roth, M.D., of Armour Laboratories, for valuable assistance; and to the following physicians of Wesley Memorial Hospital: Drs. Mary Karp, Jerome Head, Theodore Hudson, Edward Avery, Paul Rhoads, Jesse Waller, and Earl Zaus.

BIBLIOGRAPHY

1. Burleson, J. S.: The use of trypsin in postoperative anorectal surgery. Am. J. Proctol., 3:59 (Mar.) 1952.
2. Chandler, B. F.: Medical debridement by enzymatic action. U. S. Armed Forces M. J., 3:1209-1218 (Aug.) 1952.
3. Limber, C. R.; Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: Enzymatic lysis of respiratory secretions by aerosol trypsin. J.A.M.A., 149:816-821 (June 28) 1952.
4. Madden, J. F., and Ravits, H. G.: Enzyme debridement of indolent infected cutaneous ulcers. J.A.M.A., 149:1616-1619 (Aug. 30) 1952.
5. Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: The Tryptic Debridement of Fibrinopurulent Empyema. Surgical Forum, 1950 Clinical Congress of The American College of Surgeons. P. 17-24. Philadelphia: W. B. Saunders Company, 1951.
6. Reiser, H. G.; Patton, R., and Roettig, L. C.: Tryptic debridement of necrotic tissue. Arch. Surg., 63:568-575 (Oct.) 1951.
7. Roettig, L. C.; Reiser, H. G.; Habeeb, W., and Mark, L.: The use of trypsin in chest diseases. (Presented at American College of Chest Physicians, Atlantic City, June, 1951). Dis. of Chest, 21:245-259 (Mar.) 1952.
8. Samuels, S. S.: Tryptar in the treatment of diabetic gangrene. Angiology, 2:589-590 (Dec.) 1951.
9. Unger, L.: On use of trypsin in bronchial asthma and related chest diseases. The Letters of the International Correspondence Society of Allergy, Series XV, p. 25, 1952.
10. Unger, L., and Unger, A. H.: Trypsin inhalations in respiratory conditions associated with thick sputum—its use in bronchiectasis, acute atelectasis, infectious bronchitis, bronchial asthma, emphysema, and tracheotomized patients with bulbar poliomyelitis. J.A.M.A., 152:1109 (July 18) 1953.

185 North Wabash Avenue

YOU CAN'T TAKE IT WITH YOU!

The familiar saying "You Can't Take It With You" is probably older than your great-great grandfather, but it is just as true now as yesterday. Once used only in connection with money, this proverb now refers to Blood, for you can't take *it* with you either. Everyone is affected by this expression, for, rich or poor, every one has blood.

Every day hundreds of people depend on blood for their lives. In Korea our fighting men need blood every hour of the day and night. Here at home, accident and disease victims require blood in never ceasing quantities. Gamma Globulin, the disease fighting derivative of blood, is in action every day aiding grownups and children alike. Emergency blood reserves being built up by Civil Defense will help save lives . . . perhaps your very own . . . in case of an attack on this country.

Yes, you certainly can do a lot of good with a little of your blood. All it will cost you is a few minutes of your time. Give a pint today, for tomorrow may be too late to help someone live. Nothing can quite equal the satisfaction you will feel when you give your blood to help fill our country's needs. It's the kind of satisfaction that money can't buy.

Call your local Red Cross, Community or Armed Forces Blood Donor Center today to schedule your donation. It's wonderful to feel that deep-down glow of contentment in giving blood. Now is the time . . . you can't take it with you!

Editorial

The opinions expressed by the writers of editorials in the ANNALS *do not necessarily represent the group opinion of the Board or of the College.*

FROM GHENT TO AIX

This present issue of the ANNALS marks the tenth anniversary of its launching. It is appropriate to the occasion that the author of the introductory editorial of Vol. 1, No. 1, review a decade of College and ANNALS activities.

In 1943, the war was on, and many of the founding Fellows were in, or soon to go into the Armed Services. The need for a publication in whose pages the younger physicians interested in the subject could record their studies, and learn, as well, of the work of others, culminated in the founding of a journal democratically dedicated to Allergy, and serving as well for the integration of the numerous activities of The American College of Allergists. The rapidly growing subscription list attested to the fact that the ANNALS fulfilled the popular demand. The very first issue listed the three purposes for which the ANNALS was issued.

First, informally to serve the increasing number of both general practitioners and specialists who were applying and incorporating the principles of the rapidly growing subject of allergy into the diagnosis and treatment of a group of previously puzzling untreated or mistreated disorders. Its pages were liberally to be opened to the earnest, enthusiastic physicians who wished seriously to investigate new horizons in medical research.

Second, to establish departments both for papers representing the results of current scientific endeavor, as well as for articles concerned with the more practical aspects of the diagnosis and treatment of allergic disease.

Third, in accordance with the Constitution of the College, as accepted by all of its members, to help increase and broaden the scope of allergy, so that it might earn full recognition and its proper place in the edifice of internal medicine. In this regard, it is interesting to note the changing attitude towards allergy as it has grown from its earlier scope of skin testing and treatment of hay fever and asthma, to its present position, where it is more and more frequently named the "specialty of specialists."

The ANNALS was the first journal of its type to publish in each issue a section devoted to reviewing the current and pertinent background literature of each aspect of the seven subdivisions of allergy. Because the College was the first Allergy Society openly cognizant of its debt to immunologists, bacteriologists, pharmacologists, biochemists, botanists and veterinary physicians, many of whom became associates, the pages of the ANNALS reflected their manifold contributions to the subject. Although

steadfast in the tradition of publishing the results of pure research, its pages tempered the theoretical aspects of immunology and anaphylaxis with the acceptance of papers dealing with allergic principles as applied to general and other specialty practices. Its columns carried, as well, news of the meetings and programs of other societies of allergists, as well as items concerned with work in related fields of medicine.

Before the founding of the College, allergy was purposely maintained as a subject of limited interest. In an attempt to break these bonds, the Southwest and International Forums each met annually for two days. Excepting for courses given in New York, there had otherwise been no attempt to teach allergy on a national scale. The College, at its first annual meeting in Chicago in 1944, initiated comprehensive instructional courses, given by experts who dealt with every aspect of the subject. The ANNALS published those expositions deemed to be of interest to the physicians who could not attend.

When the College founded the procedure, and established the first research fellowships in allergy, and also scholarships in the subject, the ANNALS carried the news. When the present writer founded and helped weld together over thirty national societies into an International Association of Allergists (later, Allergology), the ANNALS once more told all allergists everywhere that allergy had grown from provincial to national, and then to international status. Allergy had come of age!

The impact of allergy on general medicine is not as yet fully appreciated, although it influences the direction of much specialty training. The ANNALS can continue to be a banner of allergy only as our specialty expands, both in research and in education. As the basic knowledge of the fundamental facts of our subject become more and more frequently recognized and applied to other specialties, allergy will carry a continually increasing load as a cornerstone of all medicine.

Given this, the problem of proper recognition will solve itself. Full certification will be granted.

The ANNALS, we hope, will soon carry the good news. F.W.W.

International Association of Allergology

Second European Congress of Allergology

The Second European Congress of Allergology was held in Copenhagen, May 21, through May 23, 1953, inclusive, at the University of Copenhagen. The Northern Society for Allergological Research had charge of the arrangements for this Congress and this society in turn entrusted the arrangements of the Second European Congress to the Danish Society for Allergological Research. The Danish Society announced that the Second European Congress of Allergology was held under the auspices of the International Association of Allergology. Dr. Fred W. Wittich, President of the I.A.A., participated in the Congress as a guest of honor.

Dr. Thorvald Madsen of Copenhagen and Professor Pasteur Vallery-Radot of Paris assumed the posts of Honorary Presidents of the Congress. The officers who were present were: Professor Poul Bonnevie, M.D., Vice President; Egon Bruun, M.D., Secretary General; and Secretaries Erik Andersson, M.D., P. J. Dragsted, M.D., and Michael Schwartz, M.D. President Ernst B. Salen was unable to attend because of illness; therefore, the First Vice President, Professor Dr. Poul Bonnevie, acted as Chairman of the meeting.

Vice Presidents representing other countries were as follows: Austria—W. Lindemayr; Finland—Z. Eriksson-Lihr; France—P. Blamoutier; Germany—K. Hansen: Holland—Quarles van Ufford; Italy—P. Sangiorgi; Luxembourg—C. Harf; Norway—O. Andrup; Portugal—M. Damas Mora; Spain—C. Jimenez-Diaz; Switzerland—W. Löffler; Yugoslavia—V. Spoujitch.

Delegates at the meetings of the European Council were: Denmark—E. Bruun; Finland—V. Pirila; France—B. N. Halpern; Holland—Quarles van Ufford; Italy—P. Sangiorgi; Norway—O. Andrup; Portugal—M. Damas Mora; Spain—E. Arjona Trigueros; Switzerland—W. Löffler; Yugoslavia—V. Spoujitch.

The mornings of May 21 to 23 were reserved for plenary meetings. The meetings on the afternoons of May 21 and 22, were reserved for meetings of individual sections. The Scientific Program was held at the Medico-Anatomical Institute. All reports were delivered in English, French, or German at the officers' choice. Approximately 300 were registered for the Congress.

At the official opening of the Congress, Wednesday evening, May 20, at the University of Copenhagen, the speakers were: Professor H. M. Hansen, Vice Chancellor of the University of Copenhagen; Professor Poul Bonnevie, President, Northern Society of Allergology; Dr. Fred W. Wittich. President, International Association of Allergology and Dr. Egon Bruun, President, Danish Society of Allergology and Secretary-General of the Congress Reception.

The scientific program, commencing Thursday morning, May 21, and ending Saturday, May 23, was as follows:

INTERNATIONAL ASSOCIATION OF ALLERGOLOGY

Thursday, May 21, 1953

Morning Session—9:00 a.m.

VICE PRESIDENTS P. BONNEVIE, Copenhagen, and V. SPOUJITCH, Beograd, presiding.

ALLERGY AND ADRENAL HORMONES

R. J. S. McDowall, London: "Physiological Activity of the Adrenal Hormones."
P. Vallery-Radot, P. Milliez and C. Laroche, Paris: "Les hormones cortico-surrénales dans le traitement des maladies allergiques respiratoires."
Åke Nilzén, Stockholm: "Adrenal Hormones and Dermatologic Allergy."
J. Groen, Amsterdam: "Treatment of Bronchial Asthma with Combination of ACTH and Psycho-Therapy."

DISCUSSION ANNOUNCED IN ADVANCE

Z. Eriksson-Lihr, Helsingfors: "The Correlation between Adrenal and other Hormones in Allergy."
L. Businco, Rome: "L'action de la cortisone sur les divers organes (étude histologique)."
M. Damas Mora, Lisboa: "Valeur de l'ACTH dans le traitement de quelques maladies allergiques."
W. J. Quarles van Ufford, Utrecht: "Adrenal Function Tests and Allergic Diseases."

OPEN DISCUSSION

Luncheon—12:15 p.m.
Afternoon Session—2:00 p.m.
Meeting at Medicinsk-Anatomisk Institut.
(Sections A and B meeting simultaneously)

FREE SUBJECTS

Section A

VICE PRESIDENTS P. BLAMOUTIER, Paris, and M. DAMAS MORA, Lisboa, presiding.
A. A. Israëls and Dingemanse, Groningen: "The Excretion of Neutral 17-Ketosteroids of Adrenal and Gonadal Origin in Bronchial Asthma with and without a Bacterial Bronchitis."
P. Sangiorgi, Milano: "Results of Application of ACTH in Retard Vehicle (Corticotropin Retard Roskilde) given intracutaneously in Cutaneous and Respiratory Allergy."
Z. Eriksson-Lihr, Helsingfors: "Studies on the Carbohydrate Metabolism in Allergic Diseases."
G. Capuani, E. Clerici and L. Teseo, Milano: "La réponse cortico-surrénale a l'injection endoveneuse de ACTH dans les malades de rhinite allergique au dehors et à la suite de la crise."
H. van Canwenberge and J. Lecomte, Liège: "Hormones Cortico-surrénaliennes et accroissement de perméabilité vasculaire par l'histamine chez le rat."
R. Masturzo, Napoli: "L'ACTH en quelques dermatoses allergiques."
H. Colldahl, Lund: "The Pulmonary Acetylene Elimination Capacity (P.A.E.C.) of Intravenously Administered Acetylene. A New Test of Pulmonary and Cardiovascular Function."
G. Capuani, Novaro: "Traitement de l'asthme bronchique grave par une méthode de neurolyse alcoolique."

Section B

VICE PRESIDENTS O. ANDRUP, Oslo, and QUARLES VAN UFFORD, Utrecht, presiding.
G. Filipp, Debrecen: "Allergie und Zentralnervensystem I."
A. Szentivanyi, Debrecen: "Allergie und Zentralnervensystem II."
Vera Walker, Oxford: "Manifestations of Allergy in the Central Nervous System."
Walter Roloff, Leipzig: "Die Korrelation der Atmung und der vegetativ-hormonalen Regulation—die Atmung als Grundlage allergischer Disposition."
Udo Pipkorn, Göteborg: "Erfahrungen mit Hormonhauttestungen bei verschiedenen allergischen Erkrankungen."
H. Arnoldsson and Udo Pipkorn, Göeborg: "Elektrophoretische Studien unter Androgentherapie bei Asthma bronchiale."

F. J. Farrerons & Co., J. M. Samso Dies, J. Vila Badó and L. Pau-Roca: "Electro-encephalography in Asthmatic Children."

A. A. Israëls and N. G. M. Orie, Groningen: "Some Endocrine Observations in Infected and Non-Infected Asthma."

Tabart, Paris: "Allergie endocrienne."

A. Mugler, Strasbourg: "L'Action Anti-allergique des dérivés du Colchique (Colchicine, Colchicoside)."

Friday, May 22, 1953

Morning Session—9:00 a.m.

Meeting at Medicinsk-Anatomisk Institut.

VICE PRESIDENT W. LÖFFLER, Zurich, presiding.

ALLERGY AND INFECTION

E. Letterer, Tübingen: "Allergie und Infektion, vom pathologisch-anatomischen Gesichtspunkt gesehen."

P. Bordet, Bruxelles: "Données immunologiques concernant l'allergie au cours des infections."

C. Jimenez-Diaz and E. Arjona, Madrid: "Le rôle des infections dans l'étiologie des maladies allergiques."

DISCUSSION ANNOUNCED IN ADVANCE

V. Danilovic and V. Spoujitch, Beograd: "L'asthme et infection."

H. van Marken Lichtenbelt, Zeisten, and W. J. Quarles van Ufford, Utrecht: "Some Observations during Anti-infections Therapy of Allergic Diseases."

J. Duchaine, Bruxelles: "Allergy and Infection."

Felix O. Höring, Worms: "Hyperergie bei zyklischen Infektionskrankheiten und ihre Therapie mit spezifischen und unspezifischen (Pyrifer, Cortisone) Massnahmen."

N. G. M. Orie, Groningen

R. Frouchtman, Barcelona: "L'inflammation bronchique dans l'asthme infectueux."

Luncheon—12:15 p.m.

Tuborg Brewery, Copenhagen

Afternoon Session—2:00 p.m.

Meeting at Medicinsk-Anatomisk Institut.

(Section A and Section B meeting simultaneously)

FREE SUBJECTS

Section A

VICE PRESIDENTS KARL HANSEN, Lübeck, and P. SANGIORGI, Milano, presiding.

George L. Waldbott, Detroit: "The Mechanism of Allergic Non-Infectious Pneumonitis."

Diether G. R. Findeisen, Dresden: "Erfahrungen mit der Aerosolinhalationsbehandlung des infektionsallergischen Asthmas."

S. Bergman and H. Colldahl, Lund: "A Comparison between the Bacterial Flora in Sputum and in Bronchial Secretions in Patients with Bronchial Asthma."

H. Schmidt, Marburg: "Die Rolle der Autoantikörper für das allergische Geschehen."

K. Hansen, Lübeck: "Ueber den Prausnitz-Kustnerschen Versuch."

R. Schleinzer, Lübeck: "Ueber den Prausnitz-Küstnerschen Versuch. Ergebnisse bestimmter Varianten seiner Auslösung."

O. Midttun, Sunndalsøra, Norway: "Anaphylactic Death Following Injection of Allergentract by Sensibilisation."

J. Hugues and J. Lecomte, Liège: "Étude microcinématographique des réactions allergiques locales (film)."

Section B

VICE PRESIDENTS Z. ERIKSSON-LIHR, Helsingfors, and C. HARF, Luxembourg presiding.

B. N. Halpern and Mlle. M. Briot, Paris: "Étude des polymères comme substances histamino-libératrices."
Z. Ovary, Rome: "A New Method of Differentiation of Heterophyle and Isophyle Antibodies in Rabbit Antisheepsera."
L. Buscinco, Rome: "L'action antianaphylactique de la moutarde azotée."
Fr. Kogoj, Zagreb: "Superponierte Tuberkulin und Trichophytinreaktionen."
J. Alberty, Göttingen: "Experimentelle Untersuchungen über den Mechanismus der anaphylaktischen Reaktion und die anaphylaktische Wirkung von Atropin und Tripelendiamin."
C. Cavallero, Milano: "Plasma Cells and Somatotrophic Hormone."
R. Masturzo, Napoli: "La Vitamine B_{12} synthetique en quelques dermatoses."
C. Jimenez-Diaz, J. Segovie and E. Arjona, Madrid: "Nouvelle technique de la microprécipitin réaction."
G. Biozzi, B. N. Halpern and B. Benacerraf: "Condition Influencing the Local Fixation of Antibodies in Passive Cutaneous Anaphylaxis of the Guinea Pig."

Official Banquet—7:30 p.m.

Den kgl. Skydebane.

The banquet at the beautiful Den kgl. Skydebane was fully attended and was marked with a wonderful spirit of cordiality and enthusiasm.

Saturday, May 23, 1953

Morning Session—9:00 a.m.

Meeting at Medicinsk-Anatomisk Institut.

VICE PRESIDENTS C. JIMENEZ-DIAZ, Madrid, and W. LINDEMAYER, Vienna, presiding.
W. Löffler, Zurich: Löffler's Syndrome.

OPEN DISCUSSION

Rosa Augustin, London: "Isolation and Characterization of the Active Components of Grass Pollen Extracts."
Z. Ovary and F.d'Ermo, Rome
Fred. W. Wittich: "The Present Status of Drug Therapy in the Treatment of Allergic States."
Round-Table Conference: "The Problem of the Specificity."
A. Tzanck, Paris, B. N. Halpern, Paris, A. Fagraeus, Stockholm, Ouchterlony, Gothenburg, E. Bruun, Copenhagen

PRESIDENTIAL ADDRESS

Limited space will not permit the reporting of the abstracts of the various topics and discussions presented. Proceedings will be published either in extenso in the proceedings of the Acta Allergologica commencing with Vol. VI supplementum III or subsequently in one of the ordinary fascicles of the Acta.

This was the first European Congress held under the auspices of the I.A.A. All the national societies of Allergy in existence are now affiliated with the mother organization, and the future work in allergological research rests upon the international co-operation in the common cause.

Many of the most outstanding scientists of Europe who have furnished the basic research for all our phenomena and immune mechanisms were present to participate. Also a majority of the Executive Committee of the International Association attended the Congress to lend its support and sanction. Truly, with such recognition, the I.A.A. should officially represent those working for a common goal of promoting educational and scientific research in allergy throughout the world.

Constitution and By-Laws

CONSTITUTION

ARTICLE I—NAME

The name of the organization shall be THE INTERNATIONAL ASSOCIATION OF ALLERGOLOGY (hereinafter referred to as THE ASSOCIATION) and the Association shall be governed by these Statutes in accordance with Article 60 and the following articles of the Swiss Civil Code and shall be incorporated in accordance with Article 60 of the aforesaid Code.

ARTICLE II—INCORPORATION

The incorporation of the International Association of Allergology shall be in Zurich, Switzerland.

ARTICLE III—PURPOSE

The object of this Association shall be to advance the knowledge of allergy and of related fields, and to implement the dissemination of this knowledge through International Congresses on Allergy, and by other means.

ARTICLE IV—MEMBERSHIP

Section 1. The Association shall be composed of two types of membership—Societies—and individuals of countries in which no such Societies exist. National Allergy Societies or other national organizations interested in allergy shall be eligible to join as Society members. The right to vote shall be held only by the duly appointed Delegates of the Member Societies. The right to hold office shall be limited to any member of a component Society in which he has voting power, and any individual member of the IAA.

Section 2. All members of component Societies who have the right to vote in their Society shall automatically become members of the IAA. Individual physicians and others who have made significant contributions to the field of allergy, and who reside in countries where no allergy Society exists, may be elected to membership. Members shall consist of (a) Members, and (b) Honorary Members.

ARTICLE V—OFFICERS

Section 1. The Officers of The Association shall consist of a President—a President-elect—and a First, Second, and Third Vice President (of whom the First shall reside in the country of the next Congress)—a Secretary-General—and a Treasurer. Officers shall be elected only from members of the Association. The Officers shall serve one term, from the end of one Congress to the end of the following Congress. The President and the Vice Presidents cannot be re-elected to the same office. The Secretary-General and the Treasurer may be re-elected to not more than four successive terms, and cannot hold the same office thereafter.

Section 2. The House of Delegates shall be composed of one (1) Delegate from each member Society, and shall also include the Officers of the International Association. The Delegates shall be elected or appointed by their respective Societies, and may maintain membership in the House as long as their Society wishes. The President of the IAA shall continue as Member of the House of Delegates for one term after the termination of his Presidency.

Section 3. The Executive Committee shall be composed of twelve (12) members—the President—the President-elect—three (3) Vice Presidents—the Secretary-General—the Treasurer—the immediate Past President—and four (4) Members-at-

Large, elected by the House of Delegates. The Members-at-Large shall serve for one term, may be re-elected for one succeeding term, but cannot be re-elected to the same office thereafter.

Section 4. At the first election in 1951, there shall be elected a President—a President-elect—three Vice Presidents—a Secretary-General—a Treasurer—and five Members-at-Large.

ARTICLE VI—DUTIES

Section 1. The House of Delegates shall constitute the governing body of the Association. Its duties shall be election of member Societies, individual members, and Officers. It shall formulate By-laws, rules, and regulations, and shall have all judicial and executive functions common to a scientific organization. It shall have final control over the policies and affairs of the Association, and over the actions of the Executive Committee, and of all other Committees which may be appointed.

Section 2. The Executive Committee shall conduct the usual business in the intervals between meetings. It shall act on applications for Society or individual membership, and submit them to the House of Delegates. It shall recommend the time and place of the meetings. In case of war or other emergency preventing action by the House of Delegates, the Executive Committee may take over the functions of the House of Delegates and shall continue in office until the emergency is over, and until a meeting of the House of Delegates can be held. Its actions during such emergency shall be subject to approval or disapproval of the House of Delegates.

Section 3. The President shall preside over all meetings of the House of Delegates, and of the Executive Committee. He shall be Chairman of the Program Committee. He shall be privileged to invite guests to the Scientific Meeting. With the consent of the Executive Committee, he shall appoint the members of the Special Committees. In his absence, the First—Second—or Third Vice President in order shall act for him.

Section 4. The Secretary-General shall keep records of the meetings of the Executive Committee, and of the House of Delegates. He shall keep lists of all members. He shall notify Societies and individuals of their election. He shall prepare an Annual Report dealing with the activities of the IAA, and submit it to the Executive Committee and the Presidents of the component National Societies. He shall send out notices of meetings, and other communications.

Section 5. The Treasurer shall receive dues and all other moneys and shall pay all debts therewith. He shall render a yearly Financial Account to the Executive Committee, and shall also present an Account to the House of Delegates, which shall also be communicated to the Presidents of the component National Societies at the Congress.

ARTICLE VII—ELECTIONS

Section 1. Election to membership of additional National Societies is achieved by the following procedure: (a) Formal application by the Officers and Executive Committee of the Society applying. (b) Action by the Executive Committee of the Association. (c) Affirmative vote of a simple majority of the House of Delegates present at the meeting, or a majority vote by mail.

Section 2. Election to individual membership is achieved by the following procedure: (a) Formal application to the Secretary-General. (b) Action by the Executive Committee of the IAA. (c) Approval by a simple majority vote of the House of Delegates present at the meeting, or a majority vote by mail.

Section 3. The Officers and other members of the Executive Committee shall be elected by the House of Delegates at its regular business meetings. The manner of election shall be as follows: A Nominating Committee consisting of twelve (12)

Delegates, each a member of a different member Society, shall be appointed by the Executive Committee at least twelve (12) months prior to each meeting of the House of Delegates. This Committee shall consist of Delegates: 3 from Europe, 3 from North America, 3 from Central and South America, and 3 at-large. No component Society shall have a member on the Nominating Committee for two successive terms. In case there are insufficient numbers of members available from any of these geographic divisions, the deficient members are to be chosen from other territories. The Nominating Committee shall submit nominations for the Officers and for members of the Executive Societies at least ninety (90) days prior to the meeting. Nomination for Officers and Members-at-Large of the Executive Committee must be from the list of members of the Association. At the time of election of Officers, additional nominations may be made by Delegates from the floor. A majority vote of the members of the House of Delegates shall constitute an election,

Section 4. The name of the Delegate for the ensuing term shall be presented to the Secretary-General by each Society no later than six (6) months before the next meeting. Each member Society shall have an accredited Delegate assigned to the IAA at all times, and shall fill any vacancy among the Delegates within ninety (90) days.

ARTICLE VIII—VACANCIES

In the event of a vacancy among any of the Officers, the Executive Committee shall have the power to fill the office for the expired term.

ARTICLE IX—SUSPENSIONS

A member or Society may be removed from membership in the Association for any action considered inimical to the best interest of the Association. Such expulsion requires the following procedure: (a) A written complaint filed with the Executive Committee by three (3) Delegates. (b) The opportunity presented to the Society or member to defend itself or himslf in person or writing before the Executive Committee. (c) If the Executive Committee considers the complaint justifiable, the House of Delegates will be asked to act as a Trial Board. A three-fourth (¾) vote of the House will be required for expulsion.

ARTICLE X—AMENDMENTS

The Constitution may be amended by a vote of two-thirds (⅔) of the Delegates present at a regular meeting, provided that notice of the proposed amendment is given by registered letter to the Delegates at least ninety (90) days before the meeting at which the vote is to be taken. A proposed amendment must bear the signatures of at least five (5) duly appointed delegates before it can be distributed.

BY-LAWS (IAA)

ARTICLE I—MEETINGS

The Association shall hold regular scientific, educational and business meetings, to be called CONGRESSES, at four-year intervals. Special meetings of the House of Delegates may be called by the President, or any five (5) members of the Executive Committee, or by one-fourth (¼) of the number of the Delegates.

ARTICLE II—QUORUM

Sixty (60) per cent of the members of the House of Delegates shall constitute a quorum for the transaction of business of the Association at regular and special

meetings. In the absence of a regularly constituted Delegate, the Executive Committee of the Society concerned, or its President, together with its Secretary, may name an Alternate Delegate. A Delegate may name a proxy who must be a member of the IAA to vote for him.

ARTICLE III—FINANCES

Each Component Society and individual member shall pay annual dues.

Section 1. A Finance Committee of three (3) members shall be appointed at each Congress. The function of this Committee shall be to investigate the budget expenses—the estimated income—recommend dues—and investigate sources of income.

Section 2. The minimum dues of component Societies and of individual members will be in accordance with the need of the budget. The Finance Committee will submit such proposed dues to the House of Delegates for acceptance. Approval of the amounts of such dues for the four ensuing years will require a two-thirds (⅔) affirmative vote.

Section 3. An Auditing Committee of three (3) Delegates representing different Societies shall audit the Treasurer's accounts at least for each Congress, and at any other time it pleases, on seven (7) days' notice.

ARTICLE IV

The Secretary-General shall furnish a copy of the Constitution—a Roster of the member Societies and their Officers—and a Roster of the individual members—to all component Societies and Delegates of the Association. He shall keep a list of the Founders of the International Association of Allergology.

ARTICLE V—SPECIAL COMMITTEES

Special Committees, including a Program Committee, shall be appointed by the President, with the approval of the Executive Committee. The Program Committee shall consist of at least five (5) members of the IAA, with the President as Chairman.

ARTICLE VI—PENALTIES

A Component Society which fails to send Delegates or name proxy Delegates for two successive terms—or which fails to pay dues for four successive terms—may be dropped from the IAA, but may be reinstated upon payment of such passed dues.

ARTICLE VII—APPLICATIONS

Applications for individual membership shall be made on an application form provided by the Secretary-General. It shall have the endorsement of three members. Applications of Societies for membership in the IAA shall contain the names of its Officers and Executive Committee, and shall include a copy of the Constitution of the Society. Applications must be acted upon by the Executive Committee and Delegates within eight (8) months.

ARTICLE VIII—CREDENTIALS

The Secretary-General shall review the credentials of Delegates at meetings, and shall provide each with a distinguishing badge, required for admission to the business meetings.

ARTICLE IX—HONORARY MEMBERSHIP

Honorary Membership may be conferred upon individuals who have made significant contributions to the study of allergy. They shall be granted by the Exec-

utive Committee, and approved by a majority vote of the House of Delegates. They shall be exempt from dues, and may neither vote nor hold office.

ARTICLE X—COMMUNICATIONS

The Secretary-General shall send the communications to the Editors of all Allergy Journals, and to the Presidents of all National Societies connected.

ARTICLE XI—PROCEEDINGS

The Proceedings of each Congress shall be published in uniform volume form, and made available to all members of the IAA, and placed, as well, on sale.

ARTICLE XII—ORDER OF BUSINESS

The Order of Business of the House of Delegates shall be as follows:

1. Call to order
2. Presentation of credentials
3. Reading of the Minutes
4. Unfinished business
5. Report of Committees
6. Financial Report
7. Election of members
8. New business, including time and place of next Congress
9. Nominations
10. Election of Officers by secret ballot
11. Induction of Officers
12. Adjournment

ARTICLE XIII—PARLIAMENTARY PROCEDURE

All parliamentary procedure not stated in the Constitution or By-laws shall be guided by Rules of Order and customs prevalent in the country in which the Congress meets.

Progress in Allergy

REVIEW OF MISCELLANEOUS ALLERGY
1952

LAWRENCE J. HALPIN, M.D.
Cedar Rapids, Iowa

Because of the widespread coverage given by the authors of other reviews, preparation of this miscellaneous section becomes more difficult with each passing year. The average physician interested in literature dealing with allergic diseases has two outstanding journals from which to choose most of the material that he will read. It is the primary purpose of this miscellaneous review to bring to the attention of the allergist important and worthwhile articles that appear in these journals and in others not devoted primarily to allergic diseases. In this same line, it should be noted that an attempt has been made to be quite selective and to furnish definite comment on the articles that are included in the following pages. For clarity, sectional headings have been given as follows: General Interest, Gastrointestinal, Respiratory, Dermatological, Infection, Headaches (Nervous System).

RELATED TO GENERAL INTEREST

A recent editorial[36] is devoted to the establishment of a foundation for the allergic diseases. Such an undertaking has long been the desire of those men who realize that in some areas asthma alone has caused more disability than has hypertension or heart disease. In spite of this important feature, the allergic diseases have received relatively little attention in the development of specialized facilities for treatment, research, education or investigation. Adequate research in allergy can only be financed by a concerted effort on the part of all men interested in this specialized field of medicine. In order that our present knowledge of allergy may be extended and to facilitate the training of young physicians, the interest of the medical profession and that of the general public must be aroused. The board of medical trustees for the foundation of allergic diseases is made up of men from the Academy and the College. This foundation will function independently of either organization. This editorial calls for a unity of action which can result only if this board operates as individual representatives of the medical profession in its entirety, rather than as a delegation from either existing allergy society. Such a foundation deserves the good will and support of all patients with allergic disease and from all physicians who treat these discomforting or disabling illnesses. Brown[19] has very adequately reviewed the field of allergy. He states that the first and basic form of allergy is probably anaphylaxis. It is a fundamental fact that a complete understanding of this form of allergy is the one feature which enables the physician to treat allergic disease in human beings by injection therapy. This is primarily based upon a knowledge that the procedures necessary for desensitizing, shocking to kill, and shocking to make refractory, differ only in the amounts used and the

time interval between exposures. The typical patient of the second group of allergic conditions—the atopic group—usually has a strong family history of allergy and consistently presents more than one allergic manifestation. These atopic phenomena become manifest when the sensitive tissue of the patient comes into contact with an atopen by ingestion, injection, inhalation or by direct contact. This association provides for the lesions to be reversible in the early stages. It is in this period of illness that the allergist is of greatest value both as a diagnostician and as a therapist. When the lesion has become irreversible the discovery of the causative substance or substances is usually of little value. Brown feels that skin tests can be only as adequate as are the testing solutions. In contact allergy the sensitized tissue must be adequately exposed to the causative substance or allergen by direct contact. Such substances are not true antigens. Drug sensitivity, on the other hand, is almost an entity in itself. A drug reaction is never caused by an overdose of the drug, as this is defined as toxicity. Exaggerated pharmacological responses are really expressions of idiosyncrasy rather than true sensitivity. Almost every drug available to the physician or patient today is capable of producing some degree of sensitization. A drug sensitivity may prove its presence by the production of respiratory symptoms, by the appearance of gastrointestinal complaints, by skin manifestations or by lesions in almost every organ or system of the body. It is seldom that a patient with a definite history of drug sensitivity is aware of his first ingestion or exposure to that drug. The allergic manifestations of drug sensitivity may remain with the patient for many weeks; and although there has been only one exposure, dramatic relief should not be expected to follow upon elimination of the suspected drug. Patients sensitive to infection are problems in themselves. These persons are also sensitive to fungi and to viruses which make the problem even more complex. This author discusses further the typical reactions of allergic origin that may be seen in various organs or systems of the body. He emphasizes the fact that allergy itself is a great mimic, and that such a basis for disease must be suspected in any atypical patient who possesses a strong personal family history of allergy regardless of the location or type of his present symptoms. Such a strong suspicion on the part of the physician will lead to simplification of treatment and occasionally dramatically successful therapy.

The study of clinical allergy really began after a thorough understanding of the phenomena of anaphylaxis had pointed the way. White[125] has pointed out two outstanding errors that have invaded the literature on allergy. The first error is listed by the author as the impression that allergy and anaphylaxis are identical. The second error is that the accuracy of diagnosis in pollenosis is due to the accuracy of skin test data. It is upon these two incorrect facts that additional fallacies are based. These additional fantasies are listed as follows: allergy is easily demonstrated; skin tests are accurate; the manifestations of allergy are pathognomonic; small doses of allergen are symptom producing; and desensitization will protect against skin test positive inhalants. White feels that skin tests are unreliable methods of diagnosis and their evaluation by allergists is frequently misapplied, both as to its diagnostic and therapeutic benefit. He has made a successful attempt to present evidence to re-evaluate the facts and to place fact and fallacy in their proper perspective. Such misunderstanding and lack of information about the general subject of allergy is further discussed by Crandall.[29] Though he

covers the subject with a good degree of thoroughness, he does fail to mention the importance of having good test extracts in doing any investigative procedure. He discusses the number of tests that might prove to be adequate in any investigation and considers that the proper interpretation of skin tests must be correlated with the history.

It is his impression that one of the major reasons for dissatisfaction on the part of both patient and physician in the treatment of allergic diseases is the use of stock solutions of treatment material in desensitization. He prefers the prepared antigens which are derived primarily from the materials to which the patient clinically reacts. It is his impression that practically all patients who suffer from any severe allergic disease will be found to be highly emotional. An investigation into these emotional states is considered as part of his therapeutic program. An encouragement for the patients to talk about themselves is of great assistance in interpreting the psychogenic factors that may be involved. He advocates the use of psychotherapy in treating allergic patients if an emotional factor is of importance. It is the impression of this reviewer that such psychotherapy should be in the hands of a trained psychotherapist or psychiatrist rather than in the hands of an allergist. Crandall does admit, however, that psychiatry in no way replaces the basic concepts of proper allergic treatment; and that though emotional tension may play the part of an aggravating factor in allergic conditions, such emotional tendencies are seldom, if ever, the primary causes of allergic diseases.

A plea for a closer correspondence between cause and effect is the subject of a very interesting and recommended editorial.[37] The history of medicine has demonstrated very clearly that those who do insist upon a proven one to one correspondence are more often right than wrong. This is particularly applicable to the fields of physiology and immunology. The basis for the "one to one" editorial is the quandary in which those physicians find themselves who do not, *in toto*, accept the present-day theories of psychoanalysis as applied to allergic disorders. The advocates of maternal rejections as a primary factor of childhood allergic disease would do well to recall that the allergic child suffers exacerbations of his illness because of an exposure to his allergen, as physiological states, and as psychological responses of which maternal rejection may be one. It was the opinion of this editor that if the exposure to the patient's allergen were eliminated the causes, namely the physiological and the psychological responses, would operate rarely if at all. The proof that exposure to ragweed will produce immediate responses in the sensitive child are certainly definite causes and effects. On the other hand, the appearance of bronchial asthma because of maternal rejection is not a definite answer to the patient's complaints. A close perusal of this one article is well worth the time of anyone practicing allergy today. Baldwin[8] has stated that medical education in the allergic diseases at the undergraduate and graduate levels is entirely inadequate. It is only through the combined efforts of all physicians interested in allergy that a better provision for adequate education of public and physicians can be accomplished. The importance of allergic diseases is indicated in the statement that there are several millions of people in the United States who suffer from clinical allergy of sufficient degree to warrant adequate investigation and therapy. This problem of disabling allergic diseases is of importance not only to the civilian population, but also to the military services. This is further emphasized when the realization is noted that there are only

thirteen institutions in the United States approved for training of residents and fellows in allergy.

In an address before the section on allergy of the California Medical Association, Crandall[30] stated that good public relations between the allergist and other physicians are of vital importance to the specialty. Each allergist should make this a matter of personal concern. It is important that good relations should be established and maintained not only between other physicians and allergists but also between the public and allergists. He points out that all men practicing allergy should make a definite effort to explain, rather than to conceal, the diagnosis and treatment of allergic diseases. It is not sufficient to make a diagnosis and institute therapy without explaining to the patient the nature of allergic sensitivity. This should include the procedures that have been necessary for diagnosis as well as steps that will be taken to establish relief or an eventual cure. Establishing relations between one allergist and another is of equal importance in the opinion of this reviewer. It is quite unnecessary on many occasions to repeat all investigative work that has been done by a fellow allergist, if such investigative procedures are considered to be adequate and basically sound. It might be wise for the second allergist to recheck some findings, but to repeat all procedures is a needless expense. Such close relationship between allergists could be more readily established if there were sources for standardized extracts. The lines of thought in allergic management could then be standardized to some extent so that most of the fallacies and fads of this specialty could be eliminated or avoided.

In answer to a query[87] regarding the spreading of the allergic base, most of the four consultants to whom this question was directed were in agreement. The problem of broadening the allergic base is certainly a complicated one and cannot be answered in simple "yes and no" terminology. The original question was based upon the medico-legal interpretation of the problem of spreading of the allergic base; this as a direct result of a marked allergic reaction totally unrelated to subsequent exposure patterns. For example, a penicillin reaction will frequently rekindle a quiescent mycotic lesion or a delayed urticarial response. In some instances this rekindling has been explained upon "broadening of the allergic base." On both clinical and theoretical grounds, there does seem to be some basis for the statement that the allergic base may be broadened. This should not imply that even though the original reaction was allergic, any subsequent recurrent or chronic eruption must also be allergic. Too often this assumption is made. It is true that secondary, acute or chronic infection may perpetuate the original lesions of allergic dermatitis. In addition to this, the interpretation of the original eruption in terms of cause is often hopelessly over-ridden by sensitization induced by local medication. This additional sensitization should not be regarded as a broadening of the allergic base. It is probably true that most patients undergo a gradual broadening of the allergic base through life, and that some persons are inflicted with an increased capacity to become sensitized to various substances and in various areas of the body.

Ratner and Silberman[89] are of the opinion that to acquire a hypersensitivity the following necessities must be present: 1. changing factors which make for a greater receptivity of the tissue for allergen, 2. the nature of the exciting substance, 3. the amount of allergen to which the patient is exposed, 4. the amount of allergen which eventually invades

the blood stream, and 5. the intervals at which exposures occur. In the 250 patients studied by these gentlemen, a positive family history of allergy was obtained in 54.4 per cent. This compared quite favorably with previous reports of 51.9 per cent of positive family histories obtained from a literature review. In the random population, about 10 per cent of the persons interviewed had complaints characterized as major allergic diseases and 50 per cent had complaints of minor allergic nature. Contrary to other opinions, the age of onset of allergic symptoms was not influenced by the frequency with which allergy occurs in the antecedents. It has been the impression of this reviewer that if both sides of the familial strain were allergically inclined then the appearance of allergic symptoms was usually noted at an earlier age. The work of these men would tend to refute this belief. No real hypothesis can be made to adequately apply Mendelian laws to allergy. In my own office, the presence or absence of a family history of allergy is of primary interest only for that reason, and is of no real assistance in the establishment of an accurate diagnosis of allergic or nonallergic disease. Ratner and Silberman do state that all individuals are potentially capable of developing an allergy. Such capability is dependent more upon quantitative than qualitative considerations if it is granted that the quantitative application is made to the amount of antigen which actually invades the blood stream. Ratner[90] feels that it is impossible to exclude insidious previous invasions of allergens in any given case of childhood allergy. He bases this impression upon the fact that an unaltered allergen may enter the blood stream by way of the skin or by parenteral injection. They may pass through the walls of the digestive tract or the upper respiratory tract and also be transmitted to the fetus through the placenta. In childhood allergy constitutional differences in these children make for a greater or lesser susceptibility to the development of an allergic disease. Because one of the most important features is the quantitative exposure, the progress of childhood allergic disease can be interrupted only by an early diagnosis, subsequent treatment and a reduction of contact with inciting substances. The eventual amelioration of allergy is based upon the ability of the body to produce enough antibodies so that they eventually reach the circulation and thus become blocking or neutralizing bodies. It is only through a thorough understanding of the mechanism of allergic disease that a possible decrease in the incidence may be accomplished and adequate care and supervision be substantiated. It must be understood that there is no single cure for allergy. Only through the continued interests and effort of physicians interested in this field of medicine will the incidence and severity of allergic diseases be diminished.

Smythe[108] has reported two patients with somewhat similar complaints. The first of these twelve-year-old patients had a long history of flexural dermatitis with recent appearance of asthmatic symptoms. In the second patient, respiratory difficulty, wheezing and cough had been noted since early infancy. Avoidance and elimination of the causative substances were strongly advised in association with hyposensitization therapy. Even though dietary management and dust control seemed to apply to both patients, home environment has to be conducive to success with elimination measures or such procedures will be worthless. Success depends upon the attempted control of home environment with careful observation and inspection by the attending physician. Nonspecific measures employed for temporary relief of any exacerbation are of the utmost im-

portance. Welsh[124] has reported the effect of allergic management on the progress of growth and development of thirty-four allergic children. Thirty-two of the thirty-four patients advanced at a satisfactory rate as determined by Wetzel Grids. Previous reports are in disagreement with these findings. In the past it has been demonstrated that disturbances of growth in allergic children, either with or without allergic management, have been the usual finding. McGuinness[74] recommends active immunization against pertussis for all infants as early as possible. This opinion is based upon the fact that pertussis is the most serious of the common infectious diseases in children and infants. Advice was also offered regarding the safety and effectiveness of tetanus toxoid. It is recommended that everyone should be given tetanus toxoid at an early age. The basis for this opinion is primarily upon the hazards of serum reactions exemplified by the administration of anti-tetanus sera. The antigens of choice for protection against diphtheria, tetanus and pertussis are the standard triple antigens available on the market today. The initial dosage should be given in an amount of 0.5 cc at three- to five-week intervals for three injections. Subsequent injections of 0.5 cc should be given at twelve to sixteen months of age and 0.5 cc at three to four years of age. It is advised that these triple antigens be given early in life. After the age of four years a greater degree of reaction is noted to the injection of multiple antigens than to single dosages. If the reaction from the triple antigen is of mild intensity then it is recommended that single antigens be used for future immunization procedures. Reactions to tetanus toxoid, however, will be found to be infrequent. It has been suggested that immunization procedures not be given in the presence of respiratory or other infections nor during the active teething stage. It must be remembered that those vaccines grown upon egg or egg embryo fluid should not be given to those patients sensitive to egg or its derivatives.

Differential diagnosis of convulsions in childhood is a large and difficult problem. Baker[7] feels that a careful history and a complete physical examination is imperative in such a differential diagnosis. In some instances, an electroencephalogram is indicated. Convulsions of allergic origin are rare in children if such electroencephalographic waves are reported as normal. However, any allergic background or allergic factor for the convulsions should be investigated and corrected. In this report, Baker enumerates twenty common causes for convulsions among which are included allergy and recurrent headaches classified as migraine. Bowen[17] takes exception to those reports which include epilepsy in the allergic field. He has seen one case (published) reported as allergic, with a later proven dignosis of glioma. At the Houston Convulsive Center, no proven instance of allergic origin could be found in the examination of over 3,000 epileptic patients. (see Davison[31]). He calls for greater conservative views in regard to the attempts to make allergy an all too-inclusive field of medicine. Personally, allergy is a convenient waste basket for too many physicians into which they discard their undesirable patients.

Milk should not always be a part of the diet of all normal infants and children. Pediatricians seem somewhat reluctant to remove milk from the diet of the patient sensitive or suspiciously sensitive to this valuable food. It is recognized that milk is one of the most important parts of the diet for infants and children. With recent and adequate milk substitutes, protein requirements for infants or children can be supplied through

these milk substitutes. Jeans[60] is impressed with the value of milk for infants and children, but does admit that it should not be considered solely as a source of calcium. It contributes most importantly to the requirement for protein as well as other essentials. Nowhere in the editorial comment is there a mention of the use and abuse of milk in the diet of allergic children.

No recent drugs have appeared on the market which can obviate the necessity for a good allergic work-up and allergic management. Such is the opinion of Siegel.[103] Of these only ACTH and cortisone have proved definitely to be useful adjuncts in the treatment of allergic conditions. The childhood dosage of these hormones is relatively large as compared with adult dosages, and is somewhat dependent on the severity of the illness. It must be remembered that these drugs are potentially just as harmful as they are of value. Close supervision is a definite necessity in their administration. The amounts of these drugs are always adjusted to the response of the patient and it is wise to use the smallest dosage that will maintain the patient free of symptoms. Under no circumstances should they be used as a substitute for past methods of allergic management, but they should be employed only as an additional tool for symptomatic relief. The addition of new antihistaminic drugs has revealed that few of those recently introduced are superior to the products that have been on the market for a longer period of time. It is wise to substitute an antihistaminic preparation of different chemical structure from one that has failed to produce a good response. Most of the severe intoxications from antihistaminic administrations have occurred in children so that the promiscuous administration of these drugs should not be advised. In childhood allergic diseases, as in adult allergic diseases, epinephrine and/or ephedrine still rank with the best drugs available for symptomatic relief. This author feels that Butanephrine does eliminate some of the unpleasant side reactions associated with the inhalation or injection of epinephrine. Siegel is noncommittal regarding the use of Piromen. He feels that the drug should be further investigated with extensive controlled clinical studies before its worth can be definitely proven. It is only recently that adverse publications are being noted in the allergy literature regarding the use of Piromen. Control studies have indicated a failure of this preparation to fulfill the beneficial effects reported by early investigators. In answer to a questionnaire concerning the use of Piromen, Anderson[2] was not too enthusiastic with the obtained results in average nose and throat instances. This preparation had been used by him however in acute eczematoid dermatitis of the ear with fairly good findings. Waldbott[121] has found pyrogens useful in relieving acute allergic states for five to ten days. Efficacy is lost if the preparation is used for too long a time. He warns against the danger of anaphylactic shock with Piromen usage as he has witnessed two such occurrences. Though Walton and Elliott[123] were unable to directly state whether Piromen was the cause of an asthma death, they do report the unusual circumstances following the administration of Piromen. Their patient, a woman, aged thirty-one years, expired about eighty-five minutes following the injection of this nonprotein bacterial pyrogen. Intrinsic asthma had been present for about six years prior to her death. During this time she had had two courses of ACTH therapy, a radical antrum operation and other forms of medication in an effort to give her relief. No beneficial effect of any kind was experienced with Piromen therapy. After

Piromen, her condition became quite alarming when her symptoms failed to respond to repeated injections of epinephrine and intravenous aminophyllin. Autopsy findings were limited primarily to the respiratory tract. There was intense bronchial and bronchiolar obstruction due to mucous plugging and mucosal edema. This is considered to be the typical picture of sudden death from severe bronchial asthma. Others reporting[3] have been noncommittal in their use of this drug or have had too little actual experience with it to express an opinion. Samter and Kofoed[98] report experimental and clinical studies with Piromen. Observation on fifty-one patients receiving subcutaneous Piromen convinced these investigators that the compound must be of low if any antigenicity to man. They were unable to alter the skin reactivity in ragweed sensitive patients but considered this to be of practical interest rather than of clinical significance. They were disappointed in their attempts to extend relief to patients with rhinitis, bronchial asthma and urticaria. Any improvement was not spectacular. In subfebrile doses it was unlikely that Piromen had a place in the treatment of allergic diseases of the anaphylactic type. Given in sufficient amounts, the Piromen-produced fever would probably be of benefit to patients suffering from a limited number of allergic diseases responding to other types of fever therapy. They consider that Piromen can be given safely subcutaneously and that side reactions are few. They did extend some risk to the intravenous injection of Piromen. I predict that the early enthusiastic reports will be corrected to a less optimistic level as further administration so warrants.

The treatment of the geriatric asthmatic is essentially the same as that of the younger patient. Tuft[118] advises that care be exercised in the administration of extracts to older patients because constitutional reactions are more easily induced. Asthmatic symptoms, following administration of pollen extracts in overdosage, are usually more prolonged and more disabling than noted in younger individuals. He disagrees with the impression that all asthma beginning after the age of forty is of the infectious or intrinsic type. Though food sensitivity is not an uncommon cause of symptoms in the older patient, sinus disease is rarely of significance in the etiology of geriatric asthma. This latter statement is qualified by the exception that sinus disease accompanied by frank purulent discharge may be a factor in the production of asthmatic symptoms in the elderly patient. Various types of cardiac and intrathoracic pathology must be differentiated from allergic bronchial asthma in this age group. Cardiac asthma may occur independently of, or associated with, true bronchial asthma. He discusses the various conditions which may simulate asthma. This list is longer for the elderly patient than for the younger patient. Mediastinal tumors, hypertensive cardiovascular disease, chronic bronchitis, and chronic emphysema are conditions that are commonly mistaken for or associated with bronchial asthma. An adequate history and thorough physical examination are usually required to make an accurate diagnosis of asthma in the elderly patient just as these procedures are of importance in the younger individual.

The successful management of allergic disease is dependent upon the identification of the causative factor or factors and their successful elimination or the specific therapy of these substances. One of the most satisfactory means of determining the causative agent in atopic disease is doing skin tests. Certain limitations, of course, are identified with any laboratory procedure. With the preliminary and thorough history, the

suspected agents can be confirmed in many instances by the determination of a positive reaction either by scratch or intradermal skin testing. Sheldon, Mathews and Lovell[102] point out that the history is of threefold value. It may bring out information to show that the patient's disease is one in which skin tests will be of no assistance in establishing the diagnosis. Secondly, the patient may identify sea foods, nuts, egg, mustard or certain other potent allergens for which no testing may be necessary or may even be hazardous. The history in many cases will narrow the suspected substances to a small group and tests may be done for these materials for confirmatory reasons with the elimination of other unnecessary tests. These authors list twenty-three of the commonest allergens for a routine survey. These materials, which might be classified as a screening test, include the following: egg, wheat, milk, potato, navy bean, chocolate, nut meats, sea foods, vegetable gums, cotton seed, flax seed, kapok, pillow dust, mattress dust, furniture dust, weed pollen, grass pollen, tree pollen, alternaria, cat dander, dog dander, cattle dander, and hog dander. Sensibly, they recommend that the scratch test always be completed before any intradermal testing has been instituted. Complete control over an unpleasant reaction is furnished with scratch tests. With the intracutaneous, the injection of the material irrevocably takes any unpleasant reaction from the hands of the physician. These authors advise that mustard, cotton seed, flax seed, ginger, buckwheat, mushroom, sea food and nuts never be used for intradermal testing as they are considered to be highly explosive allergens. Further discussion is submitted regarding the various techniques used in performing different methods of skin testing. They are of the impression that the house dust allergen is a specific one although such specificity may be derived from many sources. In the midst of the confusion that still exists regarding the interpretation of food skin tests, these men believe that the most reliable method of determining clinical sensitivity to a food is based on trial and error procedures. Utilization of elimination diets or food diaries is recommended. They wisely point out the close relationship that is often noted between milk and beef, chicken and egg, and mustard and flax seed. Food tests in themselves should be used only for a guide in the determination of any subsequent dietary management. Positive or negative reactions are not in themselves diagnostic of the presence or absence of clinical sensitivity. Friedewald[46] studied 1,900 private allergic patients. He encountered no deaths nor any serious reactions from doing 131,865 skin tests on these patients. The safety of the procedure seemed to be entirely dependent upon a few precautions which were observed. He is adverse to testing a patient to any food or inhalant for which a known clinical sensitivity exists. The questionable agents should first be tested by the scratch. If the results were then negative, intradermal testing could be the next undertaking. In my own office, scratch testing is used almost exclusively in all patients with intradermal testing only employed for further screening or rechecking after completely negative scratch tests have been determined. Friedewald feels that it is quite questionable whether one is justified in routinely testing allergy patients to many foods either by scratch or intradermal method. It is his impression that a positive food test had less than 25 per cent chance of being clinically important. He considers the best diagnostic approach to an allergic problem to be a very careful history of the events, conditions and other factors relating to the present complaints. Only in the absence of any clues of importance in the history

is skin testing to be considered as a short cut to finding or identifying the offending agent or agents. It is with this in mind that Friedewald decides that skin testing is worth the effort since it very often serves as a short cut to the identification of the causative substances.

The failure of allergists to agree among themselves on suitable specifications for the standardization of allergenic extracts is the principal reason for much controversy. Probably it is this unfortunate situation that hampers the efforts of allergists to secure further recognition in their field as an important medical specialty. An interesting editorial[38] calls the allergist to task for permitting varied methods of preparation and measurement of potency to produce extracts that are completely non-interchangeable. There should be unanimity of opinion regarding the measurement of potency of allergens. Variation in the extracting fluid, the proportions of pollen to fluid or the conditions under which the extraction is completed all tend to yield results that are not parallel. The protein nitrogen method of standardization for the preparation of animal dander extracts probably offers the most practical means because the weight of such material is of no value as a measure of potency. The determination of total nitrogen is of no value inasmuch as this includes nonallergenic impurities such as urea. If standard procedures of extraction and potency determination could be established, the practice of allergy would go forward in a much more acceptable manner. Brown[20] points out that the weight per volume basis for standardization is only an apparent one unless the pollen used is entirely from one source, of equal age, equal water content and equal antigenicity. He adequately discusses the work of various investigators, reaching the conclusion that despite ingenious and excellent work, the active substance of ragweed has not been isolated; thus preventing any form of standardized pollen extracts in a simple consistent manner. In similar fashion, all experimental work to identify the antigenicity of house dust as a single source of material have been failures. Friedmann[48] has stated that no allergen has as yet been prepared in a chemically pure form. This in itself complicates the problem of standardizing allergenic extracts. Since only crude extracts are being used clinically, a multiplicity of antibodies are undoubtedly formed when such extracts are employed. He reviews the various works that have been done in an attempt to produce further or better standardization of pollen and inhalant extracts.

A subject that has been for years of particular interest to me is that of drug allergy. Because of the wide variety of symptoms that may be derived from drug sensitivity and because of the several million people who will suffer from this strange occurrence, I was particularly interested in Feinberg's[41] careful and thorough review of this subject. In this presentation he successfully co-ordinates the highlights observed clinically and experimentally. Drug effects must not be confused with true allergic disease. The first exposure to a drug may have been in utero or by the ingestion of breast milk. The amounts of a drug required to provoke an allergic reaction are extremely small and certainly in much less dosage than that required for pharmacologic effect. A reaction to a drug is dependent upon the chemical structure rather than upon the pharmacologic action of the substance. Practically every organ or system in the body can respond in some way to drug sensitivity. In my experience there is nothing more frightening than the severe, intractable asthma produced by aspirin sensitivity. The respiratory reaction of aspirin sensitivity is

immediate and alarming in many instances. Sensitivity to penicillin is recognized by most allergists today, but it is surprising how many physicians in general practice or in specialties are not aware of the delayed "serum sickness" type associated with the use of this drug. The onset of the reaction—usually urticarial in type associated with edema and arthralgia—is noted anywhere from four to ten days after the injection of the penicillin and in some instances this incubation period may be as long as five or six weeks. It has been recognized that reaction to penicillin or other drugs may continue for many weeks after the administration of the drug and after the drug apparently has been completely eliminated by the body physiology. Skin testing for penicillin or aspirin—or for that matter any of the drugs—is usually without value. No degree of reliance can be placed upon a positive or negative skin test for drug sensitivity. Some drugs are wheal-producing, particularly codeine, histamine and morphine. In contact dermatitis from penicillin however, the patch test is usually positive and is confirmatory of cause. Feinberg feels that drug sensitivity is highly specific and even more often is group specific.

The absence of any reliable method for testing sensitivity to rabies vaccine was the subject of a question in one instance.[88] It was felt that the frequency with which anti-rabies vaccination accidents occur is commonly overemphasized. All drugs when injudiciously used are potentially harmful. Serious reactions and fatalities subsequent to drug administration may be avoided by attention to a history indicative of sensitivity. Grollman[53] feels that close observation for the signs and symptoms of drug intoxication is important. Idiosyncrasy and allergic reaction are entirely different features. Toxic effects of drugs may result from over-dosage, from idiosyncrasy or from allergic reaction. This author deprecates the widespread use of some of the newer additions to drug therapy—cortisone and antibiotics—as panaceas. The importance of recognizing serum neuritis secondary to tetanus antitoxin has been emphasized by Walker.[122] His patient developed generalized edema, urticaria, fever, chills and arthralgia one week following the prophylactic injection of tetanus antitoxin. Symptomatic therapy afforded very little relief. Four days later severe pain with muscular weakness was noted in the shoulder area with involvement of both right extremities. Neurological examination confirmed a diagnosis of neuritis involving the brachial plexus bilaterally. Predominant involvement of the abductors and extensors of the right upper arm was noted. Even four months after the onset of the neuritis, marked atrophy of the biceps on the right and of the deltoid bilaterally was still in evidence.

The treatment of diabetes may be complicated by the development of a cutaneous or generalized allergy to insulin. Dolger[35] has reported that such allergy fortunately takes the usual form of a localized cutaneous reaction at the site of injection. True allergy to the insulin protein with severe generalized manifestations has been noted but rarely. Beef, pork, and sheep pancreas are the main sources of commercially available insulin while the modifiers, protamine and globin, are derived from fish sperm and beef hemoglobin, respectively. It is important to know the sources of the insulin so that in a known allergy to a specific animal protein another source of different derivation may be employed. Beef pancreas is used by Squibb to produce crystalline zinc insulin and by Lilly to make

special beef Iletin. Pork pancreas is the source of supply for Lilly's special pork Iletin. Beef and pork mixtures are used by Lilly, Squibb and Burroughs-Wellcome while Sharpe and Dohme uses sheep pancreas as the source of supply. Dolger attributes local skin reactions to one of three conditions: first, sensitization to the impurities and traces of secondary proteins produced in the manufacture of commercially available insulin; second, sensitization to the modifiers such as protamine and globin; or three, irritation by the nonisotonic buffer solution. Cresol used as a preservative has never been found to be the source of a localized skin reaction. The treatment of insulin allergy can usually be accomplished by changing the brand (and therefore the source) of insulin. This is effective only when there is a known sensitivity to the specific animal protein from which the insulin has been derived. Desensitization to insulin can be accomplished quite rapidly. The author describes the method that has been found advantageous in his own experience. He prepares three dilutions of crystalline zinc insulin, namely one to one thousand, one to one hundred and one to ten. He first administers 0.1 cc of the weakest dilution followed by an increase of 0.1 cc every half hour thereafter until 1 cc of the dilution is given. When the undiluted crystalline zinc insulin is being used in this fashion, the initial dosage is 0.1 cc (four units). This dosage is increased by 0.1 cc every hour until the optimum dosage of insulin is obtained. Antihistaminic therapy has been without value in the control of generalized allergic reactions to insulin. It is true that denaturing insulin by heat can yield a physiologically potent insulin without retaining its sensitizing properties.

Vitamin preparations are often a source of allergic reactions. Jaros, Wnuck, and deBeer[59] report that reactions to thiamine present many signs and symptoms suggestive of allergy. They feel, however, that evidence is sufficient to suggest that these reactions are actually due to chemical toxicity rather than to hypersensitivity. These toxic effects of thiamine, for example, are unaffected by antihistaminic preparations, but are reversed by injections of epinephrine, one to one thousand. Allergic individuals show no greater incidence of thiamine reaction than do nonallergic individuals. It is their impression, because this vitamin is so wide-spread throughout the body and is used so extensively that the likelihood of it being a sensitizer is very small. Most toxic reactions occur when given in overdosage. Chitwood and Moore[23] report the intravenous administration of vitamin B complex causing almost immediate circulatory collapse, a feeling of impending death and cessation of respiration in their fifty-two year old patient. Emergency measures such as the intravenous administration of epinephrine and artificial respiration were without value. This patient had received numerous parenteral injections of vitamin B complex during the preceding year and for several months prior to the reported accident. Complaints of some dizziness and weakness followed the administration of vitamin B complex by the intramuscular route. Such an occurrence could not be due to overdosage and probably was distinct anaphylaxis. Because of the protein nature of ACTH it is to be expected that sensitivity to this drug would be reported in the literature. Feinberg, Feinberg and Bigg[42] have reported generalized urticaria, edema, asthma and profound shock occurring upon the initial injection of 25 milligrams of this material. Their patient recovered. The patient had received previous ACTH therapy about one year prior to the incident reported by these men. With this initial course

of ACTH therapy she had developed urticaria after the first dosage. Skin tests with corticotropin derived from pork, sheep and beef produced whealing reactions in dilutions as high as one to ten million. Tests with muscle extracts from these animal sources failed to produce any positive reaction. On the other hand, pituitary preparations produced positive skin test reactions. These findings would suggest organ specificity rather than animal specificity. Wilson[127] has also reported shock from the use of intravenous ACTH. Within fifteen minutes following intravenous ACTH two patients developed reactions consisting of chills, headache, nausea and low back pain. Though the infusion was stopped both patients developed circulatory collapse and were acutely ill. Uneventful recoveries were made following the use of various forms of therapy. Skin tests on these patients with ACTH were reported as negative.

That the antihistaminic drugs do not control severe sulfadiazine reactions has been emphasized by McKay.[75] His patient, a nine-year-old girl, presented severe skin lesions, occular symptoms, corneal ulcers, swollen lips and ulcerations of the pharnyx. Though various antihistaminic preparations were given in both early and late stages of the illness, this author felt they were without effect in offering either temporary relief or shortening the course of the complaints. Spontaneous recovery occurred after about one month though the patient did have some loss of vision because of bilateral corneal scarring. The account that the antihistaminics have failed to relieve the symptoms of sulphonamid sensitivity would suggest that the hormones, ACTH and cortisone would be of greater benefit. However, Gilbert and Arnold[50] have reported the failure of corticotropin to prevent an acute hemolytic anemia due to sulfapyridine. It is not known how the sulfonamids will cause this blood picture. Therefore these authors believe that the described reaction can only be classified as an idiosyncrasy. The dosage used by Gilbert and Arnold in an effort to control the progressive anemia was adequate though not maximal. Some authorities support the view that "idiopathic" acquired hemalytic anemia depends upon an antigen-antibody mechanism. Hellman[57] reports a true allergic reaction to procaine amide. Her patient was given 1.5 gm of procaine amide orally, followed by 250 mg every four hours. A generalized maculo-papular erythematous rash developed after the third dose. Generalized adenopathy and an elevated temperature were readily relieved, as was the rash, by the cessation of procaine amide therapy and the institution of benadryl. The identical clinical picture again developed on a reinstitution of procaine amide therapy. A patch test with this drug was negative. Though procaine amide and quinidine are closely related, reports of reactions to the former preparation have not been readily available. An unusual toxic reaction to oral administration of quinidine is manifested as an elevated temperature. Berley and Saland[11] report two additional cases of quinidine hypersensitivity with the only alteration being an elevation of temperature. They report that it is definitely important to determine whether the quinidine given to a patient is responsible for the elevation of temperature or not. The importance rests in the correct diagnosis as to the cause of the temperature elevation. Most of the patients to whom quinidine is given are subject to bacterial endocarditis or to embolism with an associated rise in temperature. Temporary cessation of drug administration with a return of the temperature course to normal would be suggestive, at least, of quinidine hypersensitivity in the febrile response.

Recently there has been some discussion at various medical meetings concerning the possibility that fatigue, unrelated to other illnesses, may or may not be upon an allergic basis. Harms and Soniat[56] estimate that 80 per cent of patients complaining of fatigue are psychoneurotic. They do admit that such patients require a thorough physical examination and appropriate laboratory investigations. These authors mention a group of chronic debilitating diseases that must be considered in the differential diagnosis; but in this list is not included the allergic classification. Because of the high percentage of patients with fatigue being psychoneurotic in origin, these authors approach the diagnosis and the therapeutic program from the view of the psychiatrist. They advocate too, the treatment of any associated physical condition or the correction of any metabolic or physical defect that might serve to aid or increase the amount of fatigue. Most endocrine preparations are administered to these patients for the lack of any other judicious therapeutic program. They decry the use of dexedrine or benzadrine in treating fatigue, except as a temporary measure.

Considerable investigation has been made of other agents in a search for possible substitutes for ACTH or cortisone. Johnston[61] has stated that it seems probable that there are now no acceptable substitutes available for these hormonal agents. In his article he reviews the work of various investigators with steroids that have warranted considerable attention—desoxycorticosterone acetate and pregnenolone. Neither of these preparations were found to approach the therapeutic efficiency of the above-mentioned and frequently used ACTH and cortisone.

The association between juvenile cataracts and atopic dermatitis has been further emphasized by Bentolila, Vila Ortiz and Bertotto.[9] They report an incident of a twenty-one year old young woman with a history of skin disturbances throughout her life. Associated bronchial asthmatic symptoms had been noted during the three years preceding her original visit to the authors. Failing eyesight and consultation with an ophthalmologist had been experienced about one year prior to this visit. Both lenses showed opacities at the time of this eye examination. Because of the long history of atopic dermatitis and associated bronchial asthma, a diagnosis of allergic cataract was considered to be established. These cataracts of allergic origin usually appear in the second or third decade of life. Though there is no definite explanation of the mechanism for allergic cataracts, the most generally accepted hypothesis is that the allergic person has suffered a reaction in the lens with the resulting cataract. The permeability of the capsule of the lens has been disturbed by atrophy and thus the first stage of cataract formation has been completed.

Local thrombosis and hemorrhage characteristic of the Arthus phenomenon is similar to that noted with the Shwartzman phenomenon. Stetson[111] sensitized rabbits with repeated injections of ovalbumin until well-defined Arthus reaction was noted. Determinations of aerobic glycolysis were not made after the third hour because of hemorrhage and necrosis. No increase in aerobic glycolysis could be determined when the skin excised from sensitized animals was incubated *in vitro* with ovalbumin. Intracutaneous injections of meningococcal toxin was administered to rabbits sensitized to ovalbumin and thus the stage was set for the Shwartzman phenomenon. Twenty-four hours later, in a distant skin site, ovalbumin was injected. Both the Shwartzman and Arthus sites reacted within twenty-four hours with similar and almost distinct hem-

orrhage and necrosis. The Arthus reaction was somewhat delayed as compared to the Shwartzman phenomenon. An inhibition of the Shwartzman phenomenon could be obtained with nitrogen mustard because of the removal of polymorphonuclear leukocytes from the circulation. Four days later the intracutaneous injection of ovalbumin resulted in no reaction in twenty-four hours, although extensive hemorrhage and necrosis did occur within four days. In control rabbits not treated with nitrogen mustard, a typical Arthus phenomenon was noted to reach its maximum in five hours with gradual subsiding severity over a period of the subsequent forty-eight hours.

Hyaluronidase is present in or around connective tissues at all times. Rawlins[92] feels that this enzyme is liberated from damaged tissue in large amounts in any allergic inflammation of the skin. The resulting hyaluronidase is therefore available for the production of allergic edema. Since ACTH and cortisone do not function in allergic diseases by any change in specific antibody formation, this author feels that these agents overcome the action of allergic factors by being antihyaluronidase, i.e., by acting as antihyaluronidase agents. No hyaluronidase can be demonstrated in the circulation and therefore it must be in the connective tissue. Because the allergic skin inflammation is overcome to some degree by the antihistaminic agents, this author is of the impression that the antihistamines are antihyaluronidases. In allergic disease there is either an overbalance by hyaluronidase, of the building up enzymes of connective tissue, or there is a dysfunction in the autonomic nervous system and hormonal system in which there is no equilibrium.

Wieners work on Rh sensitization is of great interest to allergists.[126] While the blocking antibodies are responsible for immunity to pathogenic or micro-organisms, agglutinating antibodies appear to be the basis for hay fever, asthma and eczema. At the same time the blocking antibodies, because of their ability to traverse the placental barrier, are largely responsible for an infant's neonatal immunity. It is also true that the agglutinating blood type's specific antibody causes erythroblastosis fetalis. These latter antibodies are unable to pass through the placental barrier. In his presentation, this investigator describes the average response which occurs following a course of immunization. He is of the impression that allergic individuals constitute a selected group whose immune reactions differ from the normal.

That the total dose administered is the chief factor in histamine desensitization is the suggestion of Ambrus, Ambrus, and Harrison.[1] This is based upon their work with guinea pigs given a single large dosage of histamine after having been protected with Neoantergan. Because of the absence of antihistaminic activity in the organs of desensitized animals and the presence of a higher histamine-like activity on guinea pig ileum, it was their conclusion that this residual histamine was bound in the cells on a non-toxic basis. They considered this binding to be a protective form opposed to subsequent exposure to histamine. Histamine is the medication of choice in the treatment of multiple sclerosis according to Jonez.[62] When a definite diagnosis of multiple sclerosis has been made, some form of histamine therapy is indicated for the balance of the patient's life. Jonez institutes therapy with the standard histamine intravenous infusion of 2.75 mg of histamine diphosphate in 250 cc of normal saline. The usual rate is thirty to sixty drops per minute with ninety minutes being taken for the full administration. The routine multiple

sclerosis course at the Tacoma Clinic consists of thirty such doses, five each for the first three weeks and three each for the next five weeks. No noticeable reactions have been experienced in over sixty thousand intravenous administrations of this solution. Any reactions that might occur are thought to be due to the pyrogenic factor of improper sterilization or too rapid administration of the solution. Failures probably result from the inadequate administration of sufficient amounts of histamine or when the solution is given too late in the disease. It is quite obvious that any irreversible changes cannot be corrected by any form of therapy. Jonez is emphatic in the necessity of the patient with multiple sclerosis to avoid the use of tobacco, which is one of the strongest vasoconstrictors.

In addition to the use of histamine injections, all patients should be on complete allergy management. Environmental and dietary control is a necessity. It is admitted that histamine therapy will not cure multiple sclerosis, but it does arrest the symptoms in a great percentage of patients. This same author[63] feels that histamine administration is absolutely safe if ordinary care and intelligence are used. Self-administration of this drug either by repository or iontophoresis method is permissible. It is Jonez's opinion that histamine activates the suprarenals to bring about rapid temporary relief. It is also his impression that histamine acts as a hypo-sensitizer. Histamine is a normal constituent of the blood stream and probably originates in the bone marrow from which the granular leukocytes carry it. Code[26] states that histamine is normally contained in these granular leukocytes and is released by the addition of trypsin, papian or peptone to the blood. These additions may be made as a result of humoral antigen-antibody reaction. Though there is some evidence that eosinophiles carry histamine there is no elevation in the concentration of histamine with an increase in the number of eosinophiles in the blood stream. Jonez[64] describes the use of a repository type of histamine therapy in the treatment of multiple sclerosis patients and in the treatment of allergic patients in general. A histamine diphosphate suspension was 2.75 mg per cc in a menstruum of oxycholesterol derivatives dissolved in peanut oil. The usual institution of his treatment was .05 cc of this suspension daily given as a deep intramuscular injection. The dosage was increased at a rate of 0.05 cc per day until on the tenth day the patient was receiving 0.50 cc of this preparation. With production of any severe headache, the increase was either stopped or the dosage leveled off at that point until an increase could be tolerated without any apparent associated reactions. When a dosage of 0.50 cc had been reached, this was considered as a maintenance dosage and was given every second day. In some instances a further increase was made until a dosage of 1 cc was given. In addition to the initial use of this preparation in a variety of allergic conditions, this author used the same preparation in the therapy of multiple sclerosis. He considers respiratory histamine to be entirely safe. He even goes so far, somewhat enthusiastically I am sure, to report that repository histamine injections appear to have nearly the same therapeutic effect in allergic diseases as do cortisone and ACTH.

Ferris, Alpert and Coakley[43] gave 607 transfusions to 367 patients. To each of these transfusions, 25 mg of pyribenzamine were added. The reaction percentage on an allergic basis was 0.16 per cent. There were no pyrogenic reactions. In their control series, there were twenty allergic reactions and thirty-two pyrogenic reactions in 742 pints of blood given without pyribenzamine. Reisner[93] believes that anaphylactoid purpura is

in the same category as rheumatic fever, acute nephritis, and possibly periarteritis nodosa. It is unusual when a specific allergen can be incriminated as a cause of anaphylactoid purpura. He considers this to be representative of hyperergic vascular responses to infection. Thrombocytopenic purpura may be the result of a sensitivity reaction. Immune mechanisms have also been responsible for this form of purpura particularly where no demonstrable drug nor toxic factor can be established. Antihistamines have been of no value in hematologic allergies because they neither prevent sensitization nor the union of the antigen and antibody. The neutralization of the effects of histamine, liberated in the tissues at the site of reaction, is the only effect expected from the administration of antihistaminic preparations. Because of this, the use of antihistaminic preparations in the prevention of a transfusion reaction cannot be looked upon with any degree of success because they simply mask the symptoms of such reaction and do not prevent hemolysis from taking place. This would seem to be in complete disagreement with the first few sentences of this paragraph.

Cazort[21] is of the impression that bee sting sensitivity is a specific reaction to an individual antigen. The patient sensitive to the sting of a bee is not sensitive to the sting of the wasp. He is one of the few reporters who feel that the severe anaphylactic type of reaction is quite unusual, with the general instance of such sensitivity consisting of a temporary urticaria. When the severe bee sting reaction does occur, an alarming situation is encountered. In agreement with other reports, Cazort is at a loss to state when adequate desensitization therapy has been given. All these patients—and their physicians—are reluctant to be exposed to a clinical test of sensitivity. Little[72] also raises the question of success in prophylactic insect desensitization. He was apparently successful in ridding dogs and cats of fleas by injecting a saline flea extract in small dosages at rather frequent intervals. The importance of giving epinephrine immediately following an insect bite or sting has been reiterated by Bernton.[12] Intravenous calcium as an aid in immediate therapy of insect bite reactions is mentioned by Baird.[6] This may be given as an intravenous injection every three to four hours and relieves the edema and itching. Personally, I would rely on epinephrine to a greater degree in the acute severe reactive stage. MacLaren[76] is of the opinion—based on six extreme instances—that bee-sting sensitivity is easily and rapidly developed. He considered his patients to be adequately desensitized when they could tolerate the equivalent of one bee sting without reaction. This was accomplished with whole bee extract, giving six to ten injections once weekly. The life-saving value of epinephrine is strongly supported by Swinney[115] who thinks that antihistamines and other measures should be condemned except as palliative and supportive therapy. Talley[117] was able to control two severe reactions without epinephrine. Relief of symptoms and control of sequalae were noted with sublingual Isuprel and Nephenalin. Desensitization of the bee sting sensitive patient may, for some reason, cause the insects to search elsewhere for fun or fill. Stier[113] found that two patients so desensitized were able to expose themselves to yellow jackets without receiving a sting. It has been my impression, gained through shallow experience and the literature, that the sensitive patient seems to possess a definite attraction for the biting or the stinging insect. Goldman and Rockwell[51] have demonstrated three distinct types of allergic reaction to insect bites: urti-

carial, tuberculin, and eczematoid. Surprisingly, epinephrine is not listed by these exhibitors in their recommendations for the systemic control of symptoms. They have mentioned cortisone and ACTH.

FOOD ALLERGY

In the management of the patient sensitive to food, Clark[25] advocates the use of a four day starvation period. On the fifth day ingestion tests —one every two hours—are initiated. He has found it advantageous and time saving to have six to eight patients undergo feeding tests together as they provide company for each other throughout the day and are able to observe various clinical responses. This seems to lessen their doubts about the efficacy of the program. If a reacting food is encountered, testing is interrupted for two days. He relies upon an eosinophile count to confirm doubtful reactions. Simon[105] does not credit egg as an important causative factor in infantile eczema even though the ingestion of egg may cause urticaria and vomiting. He feels that infantile eczema is an epidermal reaction to an allergen present in the patient's own skin. Because of its universal presence, avoidance is an impossibility. Testing should be by patch technique since the basic reaction is epidermal in character. Smith[107] rates egg high on the list of causes for infantile eczema while Spearman[109] places milk, wheat, orange and chocolate as more frequent producers of these lesions. Service, Schwartzberg, Rosen, Shea and Satrang[4] all agree that, though egg is a factor of consideration in infantile eczema, milk or cereals will be found as more frequent causative substances. General agreement seems to prevail on this same subject if we include multiple answers that have been obtained to this interesting question. Cazort[22] is probably more radical or thorough in the elimination of egg from the diet than are other clinicians. His results, however, tend to support his views. He feels quite optimistic when he has an infantile eczematous patient with a marked reaction to egg. Elimination of egg at his suggestion is real and complete elimination—not only by the patient, but by the family and from the environment as well as from the diet. Cazort's degree of egg avoidance is surely worthy of actual trial in those stubborn and resistant egg sensitive cases. Bernton[13] continues his interest and interesting reports of corn sensitive patients. His present study deals with the incidence of sensitiveness to corn derivatives. His test patient was a thirty-seven-year-old woman sensitive to corn by ingestion. Corn on skin testing, however, gave negative reaction. She did admit in her history that the ingestion of corn starch was probably the worst offender of all corn products. When Bernton tested her for various corn derivatives and different types of corn meal, the only reactive skin test was one showing some erythema and itching to corn starch. Ingestion tests gave positive reactions with appearance of itching of the lips and severe asthma after swallowing one teaspoonful of corn meal. Over a period of time, this investigator determined that corn meal mush and corn starch pudding would cause asthmatic symptoms whereas other corn derivatives, such as oil and syrup, would not cause clinical appearance of any complaints. In view of the positive ingestion test and the negative skin tests, Bernton emphasized the limitations of cutaneous testing for food sensitivity. In an effort to explain the degree of reaction with corn starch, Bernton feels that there are two possible sources of the protein responsible for these reactions. There may be some residual protein in corn left over on separation of the starch

from the gluten water. Ordinary commercial starches are not entirely bacteria free and this may also account for some contamination resulting from exposure of the starch to air and water. The protein content of corn syrup is negligible because this residual protein is probably more thoroughly denatured than it is in corn starch. Though this author feels that no deduction should be drawn from a single observation—either positive or negative—he does believe corn allergy and corn derivative sensitivity are indeed open to question. There have been no ingestion tests that have shown positive reactions to corn sugar, corn syrup or corn oil when these tests have been adequately controlled.

That gastrointestinal allergy can simulate symptoms of acute abdominal pathological disease brings to mind Brown's statement, previously mentioned, that allergy is a great mimic. Blumstein and Johnson[16] report a patient whose recurrent attacks of abdominal distress were of such nature as to cause surgery with a presumptive diagnosis of acute appendicitis. At operation the diagnosis was found to be incorrect in that the appearance of the involved bowel was typically that of regional enteritis. The histologic picture, however, was found to be that of an allergic reaction. With the elimination of sea food from his diet this patient remained well and had no further attacks. The diagnosis of sea food sensitivity was determined by the occurrence of three rather severe attacks shortly following the ingestion of sea food. The authors discuss the diagnosis of gastrointestinal allergy and propose that this should be made only upon clinical standards. A cause and effect relationship between the ingestion of a food or a group of foods and the appearance of symptoms is imperative. They assert that gastrointestinal allergy occurs more frequently with other allergic symptoms than in the supposedly nonallergic individual. Loeffler's disease is usually considered by most men to be primarily a condition involving the pulmonary system. Ruzic et al[97] describe a transient eosinophilic lesion of the stomach in a patient who presented a history of Loeffler's syndrome. They offer the suggestion that past reports of Loeffler's syndrome have been too limited in that the other organs of the body are not included in these interesting lesions. Some patients who are allergic to certain foods deliberately eat these foods thus creating self-inflicted food induced allergic illness. Kaufman[66] has prepared a very interesting report on this subject. It is his impression that the allergic patient will eat such foods in times of stress. The emotional support derived from their ingestion far outweighs the disturbances that may arise from this self-inflicted food-induced allergic illness. The expression of a severe guilt feeling or the depth of a depression may force a patient to punish himself by deliberately eating the foods for which he has a known sensitivity. Secondary gains from allergic illness can also be obtained by persons who seek sympathy and support through their self-inflicted illness. Kaufman discusses the therapeutic measures by which the allergist can help a patient in this functional disease.

The rapid onset of hemiplegia following the ingestion of a light meal has been described by Staffieri, Bentolila, and Levit.[110] Associated edema, urticaria and purpura were marked but these symptoms were of temporary duration. Twenty-four hours later the attack was repeated with the same characteristics. Laboratory work, including bleeding time and blood clotting time, was all well within normal limits. The only abnormality was an eosinophile count of 40 per cent with 15 mg albumin

in the urine. By dietary management it was established that the ingestion of wheat was the causative factor, as edema and purpuric signs would appear shortly after the ingestion of wheat flour. The patient has remained free of these distressing symptoms on a wheat-free routine. That the pylorus plays a major role in allergic symptomatology of the stomach has been proven by x-ray by Fries.[49] For this investigative report the author studied thirty allergic children. Vomiting, abdominal cramping, nausea and epigastric distress had been the main complaints experienced shortly after the ingestion of small amounts of offending foods. In the control series barium began to leave the stomach immediately or within ten minutes after ingestion, whereas in the sensitive patients a delay of twenty minutes or longer was observed. Persistent or intermittent narrowing of the pyloric canal was also noted. Since the pylorus is thick and highly contractile with a narrow lumen, the allergic reactivity may be explained upon its physiological basis. Decreased muscular tone of the stomach and diminished peristalsis also were noted and may account for some of the gastric retention. Re-exposure of these patients to the causative allergen resulted in a reactivation of the same pyloric reactions. Szilard, Rauss, and Szabo[116] studied seventy patients with gall-bladder complaints. They found that the coli bacillus occurred most frequently in the duodenal secretion. Their investigations proved that the blood of patients with chronic cholecystitis contained agglutinins against homologous coli strains found in the duodenal secretions. All agglutinations occurred with homologous strains and no agglutination was noted in the control patients who were not allergic patients. These men believe that the duodenal juices contained pus which was the result of allergic inflammation rather than any coli infection. Upon administering small doses of prepared vaccine, unusual local and focal reactions did occur which tend to support their theory. A vaccine prepared from non-agglutinating, but homologous coli strains produced local toxic infiltration but did not produce any focal reaction. These authors thus feel that new light is thrown on the characteristics of chronic cholecystitis in that it is a disease of focal origin.

Ratner could not agree with the methods and findings of Rinkel and Randolph[94] because they did not present objective proof of the presence of food allergy in their patients. Because of this, Ratner[91] conceived a method of testing whereby the food in native and modified forms is tested not on the patient by oral trial but rather upon nonallergic recipients. The objective finding of a positive urticarial reaction at passively sensitized sites was the sole determinant of the reaction. There are three phases to this so-called dual ingestion passive transfer test. Blood was drawn from allergic subjects who had been found skin sensitive to food proteins and who were clinically sensitive to these same foods. When properly prepared the serum was ready for use. Nonallergic subjects were selected as recipients (after skin testing to rule out any evident hypersensitivity for food). The serum was then injected into several skin sites of this recipient to produce passive sensitization. The direct site of the test was challenged with a food protein to which the donor reacted in order to determine whether there were circulating antibodies for these specific foods. Twenty-four to forty-eight hours later the recipient ingested the modified or processed foodstuff under investigation. A positive reaction would usually occur within fifteen to thirty minutes or later and persist for several hours. If there were no reactions the

assumption was made that some change had accurred in the allergenicity of the foodstuff or that the material did not pass through the intestinal wall. Ratner has found many interesting features from this controlled study. Egg protein subjected to moist heat appeared to lose some allergenicity of the albumin and globulin fractions, but the ovomucoid fraction was not affected in this respect. Hence, any individual sensitive to the former fractions will be able to tolerate a hard-boiled egg whereas the individual sensitive to the ovomucoid could not do so. Fish proteins were quite highly allergenic in spite of subjection to moist heat. Peanut oil was shown to be nonallergenic whereas peanuts were highly allergenic. It is emphasized that with this method of dual ingestion passive transfer testing the doubtful trial feeding method should be supplanted.

RESPIRATORY

It is frequently seen that a patient with perennial symptoms of nasal congestion and nasal discharge will be of the opinion that he has an acute or prolonged head cold. Most of the physicians doing allergy today are aware of the value of nasal smears for eosinophilia. Siegel, Goldstein, Sawyer and Glaser[104] investigated the nasal complaints of 186 patients. These patients gave histories of having had frequent "colds." No significant difference in the nasal smears of patients with positive family histories could be determined in comparison with those that failed to reveal any allergic antecedents. The individuals susceptibe to what were thought to be colds did have a history of asthma or some other form of respiratory allergy in 9.2 per cent more than those without similar complaints. The impression was gained that the patient with complaints of having had frequent "colds" is usually more susceptible to allergic conditions. A causal relationship between the allergic constitution and the incidence of "colds" had been suggested. These authors did not include urticaria and angio-edema as associate major allergic conditions because these dermatologic expressions of allergy occur frequently in persons who show no other allergic manifestations. The treatment of childhood pneumonia is admittedly inadequate and therefore may be a common predicator of bronchial pulmonary disease. Finke[44] has presented some interesting discussion. The acute stage of the disease is usually resolved with a short course of antibiotic therapy, but subsequent, complicating bronchial pulmonary conditions are not averted. Complete therapy for respiratory conditions will act as a preventive measure for the development of pneumonia and other subsequent complaints. Examination of the aural secretions for eosinophiles is a valuable diagnostic measure in determining whether or not various forms of otitis are allergic in origin. Derkacki[33] feels that ractions to skin tests in these conditions can often be misleading. Greater dependence is placed upon the removal of a specific substance or the treatment with an extract of that substance in relieving symptoms. Allergy may always be assumed as a cause of otitis if the symptoms recur on exposure to the suspected material or after treatment has been discontinued. Pollen, food, drug or inhalant sensitivity is often responsible for persistent discharges after mastoid surgery or fenestration procedures. The excellent results obtained in labyrinthin hydrops with proper allergic management justify consideration of possible allergic etiology in all of these patients.

Ephedrine was the first nasal vaso-constrictor to be introduced into clinical practice. It still is the one most widely used by the physicians

today. Fabricant[40] worked with forty rabbits, instilling progressively buffered solutions of 1 per cent ephedrine hydrochloride in isotonic sodium chloride solution into the right nasal passages. The left passages served as controls. The ephedrine preparations bore a pH value ranging from 2.5 to 12.0. Gross purulent exudate was demonstrated in autopsied animals treated with solutions of ephedrine buffered to pH 3.0 to 12.0. Pathological changes in the respiratory nasal mucous membrane consisted of slight to considerable hyperemia and acute to chronic inflammation with varying degrees of suppuration. Acid or alkaline solutions were found more likely to produce traumatic and suppurative mucosal changes than were neutral solutions of this preparation. In clinical practice it is more desirable, therefore, to use a nasal vaso-constrictor which lowers the abnormal alkaline pH to a level between 5.5 and 6.5 in adults or 5.0 and 6.7 in infants and children. These figures approximate a physiological nasal pH.

Allergenic factors must always be considered in the management of maxillary sinusitis according to Harkness.[55] Allergy may be the sole cause of complaints or it may be superimposed on an infectious base. It is rather difficult to decide which is the more important factor when both infection and allergy are present. A conservative course has been advised even though radical surgery may eventually become necessary. He emphasizes the fact that the nasal mucous membrane may not be diagnostic of allergic disease in itself, as both red and pale membranes may be noted on allergic conditions. Radical surgery should be postponed in the light of an eosinophilic nasal smear, but this finding does not contraindicate the simple snare removal of obstructive polyps from the nasal cavity. Before any shrinking agent or local anesthetic is used in the preparation or treatment of patients with maxillary sinusitis, the first requisite should be a known lack of antagonism to ciliary activity. Antibiotics and sulfonamids are recommended whether they be given orally or parenterally. The prime requisites of a healthy maxillary sinus are proper aeration and ciliary activity. With the introduction of allergic methods and the use of antibiotics, Hansel[54] now postpones surgical interference until proper diagnostic procedures have been completed. He has divided the inflammatory diseases of the paranasal sinuses into three groups: infection, allergy and allergy with infection. Most important of diagnostic procedures is the examination of the nasal cytology. Hansel advocates the use of mixed respiratory vaccine for the prevention or treatment of cold; thus preventing or delaying any associated paranasal sinusitis. He uses these materials in extremely high dilutions with progressively increased dosages over a period of several weeks. The above plan of treatment was used by this author in past years. Recently he found that staphylococcus toxoid injected intracutaneously was of greater value. The ineffectiveness of virus and other vaccines in the treatment of the common cold has been the result of failure to obtain or establish an effective optimum dosage with these preparations. The matter of dosage and vaccines and extracts has long been a controversial point at most allergy discussions. There are those who follow Hansel's so-called "optimum effective dosage." There are others who believe that dosages in extremely high dilutions are without value. Dosages should be determined upon the basis of the clinical picture and the response of the patient to the amount administered.

One of the most interesting articles, with excellent diagrams showing

the pathologic and physiologic anatomy, is a publication by Miller.[79] Most hearing disorders of adult life have the original onset in childhood being due to adenoids, infections or allergic rhinitis. Changes in the middle ear frequently result from decreased nasal space or from repeated attacks of nasal inflammation. Deviation of the nasal septum with compensatory hypertrophy of the turbinates is one of the important causes of decreased nasal area. The persistence of adenoids, nasal allergy and subsequent polyps are other important reasons for decreased nasal space. Removal of nasal polyps is advised in order that the nasal pharyngeal pressure may may be kept as low as possible at all times. Miller calls attention to the importance of correcting the hypertrophied turbinate opposite the deviation when a sub-mucous resection has been performed. The nasal triad has been described as a bad deviation, hypertrophy and resulting poor nasal space. Proper allergic management following adequate investigation is recommended in these instances in order to control mucous membrane swelling and allay the eventual return of nasal polyps. Berdal[10] has carried out investigations in a number of patients on the antibody content in the fluid of nasal polyps and in the blood serum. Parallel investigations of serum and edema polyp fluid reveal a quantitative comparison between the antibody content of these sources. A positive reaction was reported at a far greater titer for polyp fluid than for the reactions noted with blood serum. This, according to the author, would suggest an accumulation of specific antibodies against certain definite allergens in the edematous polyp fluid as compared to that of blood serum. Such accumulation of specific antibodies may be assumed to depend upon a local hypersensitivity. There was a higher proportion of negative skin test reactors above the age of forty years in patients with allergic rhinitis and nasal polyps reported by Pepys and Duveen.[85] There was an incidence of nasal polyps in 17.6 per cent of those patients showing positive skin test reactions and 31.6 per cent in the negative reactors. The absence or presence of positive skin test reactions did not in any way affect the benefit received from desensitization and elimination. Recurrence of nasal polyps was adequately prevented and controlled by proper allergic management. Of 126 cases treated on the basis of clinical history and the skin test findings, seventy were sufficiently benefited to warrant continuation of therapy. Treatment consisted of dietary management, estrogenic therapy and desensitization with inhalant allergens. The changes in allergic mucosa were found to be reversible and adequate control of the allergic state did delay or prevent frequent recurrences of nasal polyps. These authors found that there was a tendency for the nasal mucosa to react to a large variety of stimuli not related to the original allergic factors.

A careful and complete allergic study with evaluation of any contributing factors will prove to be important differentiating points between allergy and true infection according to Rinkel.[95] Postponement of allergy investigation is advised in the presence of purulent secretions and elevated temperatures. Antibiotics and sulfonamid therapy are recommended before the investigation is undertaken. He feels that acute and recurrent head colds involve lowered resistance and inadequate diet. The factor of allergy should be given primary consideration. Antihistamines only delay the development of purulent secretions and the administration of minute doses of histamine have tended to alleviate allergenic sensitivity and thermal exposure. Because of the high humidity of the atmosphere in Cuba, pollen allergy is not a frequent finding among the population

of that country. de la Riva[32] states that mold sensitivity is frequent. Molds along with house dust are the major causative factors of respiratory allergy in his country. He lists the predominant molds as hormodendrum, mucor, fusarium, helminthorsporium, penicillium, rhizopus and aspergillus.

Circulation times and the effect of intravenous aminophyllin were used to help corroborate or negate a diagnosis of bronchial or cardiac asthma by Schuman and Simmons.[99] They studied seventy-five cases in which bronchial asthma was diagnosed in thirty and cardiac asthma in thirty-five. The remaining ten were considered to have both cardiac and bronchial asthma. Normal circulation times were found in those patients with bronchial asthma. The circulation time, consisting of arm to tongue period with Decholin, was above twenty seconds in those patients with cardiac asthma. Dyspnea was improved in every instance of bronchial asthma with the administration of 7½ gr of intravenous aminophyllin. The cardiac group was generally unimproved by this procedure. Therapeutic effects of aminophyllin, however, may be of some value in comparing bronchial and cardiac asthma as well as affording relief to the patient with the former disease. That aminophyllin did not afford relief to the cardiac asthmatic was a point in favor of a mechanical rather than a spasmodic basis for the pulmonary findings. A different mechanism for the production of each condition is also suggested by the adverse effect of morphine upon bronchial asthma with the beneficial result being noted in the treatment of the cardiac patient. Exposure of the asthmatic chest to radiologic technique with two x-ray photographs, one in forced inspiration and the other in expiration, has been presented by Diaz and his co-workers.[34] The inspiration roentgenograph is then superimposed upon the one taken during expiration. The changes in the diaphragm, ribs and clavicles are sketched on one plate. The mechanism of respiration and the participation of each factor involved can thus be determined. By this means, the authors feel that they can recognize the presence of bronchial obstruction, emphysema, congestion, edema and fibrosis. That symptomatic bronchiectasis and irreversible bronchiectasis are rare in the asthmatic patient has been called to the attention of the profession by Friedman[69] and Waldbott.[70] Their letters were in protest to the implication that bronchiectasis and asthma are commonly associated. Such was the conclusion of Overholt, Walker and Woods.[84] It has been accepted that in asthmatic patients with intractable complaints a search should be made for causes other than those based upon allergy. Overholt feels that a great majority of these patients are bronchiecstatic, since exploratory thoracotomy was done on twenty-seven bronchiecstatic patients and all but one were treated by excision of the diseased tissue. Of the twenty-six patients so operated, twenty were greatly improved and only seven of these required continuation of drugs affording bronchial dilation.

The importance of making a diagnosis of bronchomoniliasis by biopsy, sputum examination or autopsy has been emphasized by Orie.[83] The author contends, however, that a diagnosis of moniliasis is often a false interpretation of sputum slides and cultures. He believes that the fungus does not originate in the lung but rather is a contaminant of the sputum of the oral cavity. A breakdown of general resistance or a failure of expectoration will permit the monilia to invade the respiratory tract. When this occurs there is usually some underlying debilitating disease with resulting lung infection by the monilia being due, in part at least, to hematogenic spread. Four cases of mycosis fungoides in which pulmonary

lesions were demonstrated by roentgen examination are reported by Bluefarb and Steinberg.[14] This condition is primarily a disease of the reticuloendothelial system. Though the disease manifests itself primarily in the skin, visceral findings frequently have been noted and reported. Of the four cases reported by these authors, three were verified at autopsy. The fourth patient had clearing of these pulmonary lesions following treatment with nitrogen mustard and radioactive phosphorous. Typical pulmonary involvement is reported by x-ray to begin with hilar enlargement and a subsequent spread of the affection along the vessels. Small nodules later appear so that there is a typical picture of bronchial pneumonia noted. The apices usually remain quite clear and thus can be differentiated from tuberculosis. The mycotic infection does not enter the lungs until there is a breakdown of the hilar lymph nodes.

We all recognize the undesirable features of the nasal pharyngeal catheter and those of the more complex rubber face masks for the administration of oxygen. This was the inspiration to Segal and Herschfus[101] to develop a new type of face mask. It was designed to administer oxygen in adequate concentrations for either brief or prolonged periods. The plastic tent fits comfortably over the lower portion of the patient's face and is open widely at the forehead for the easy egress of exhaled gasses and vapors. Because of the ease of application no constant attendance nor expert supervision is necessary. Visibility, as well as breathing, is completely free and unobstructed at all times. There have been no complaints of claustrophobia or a sense of suffocation, common findings in the patient with an overall tent or a face mask. Spasm of the small bronchi and bronchioles producing obstruction and subsequently emphysema is called progressive bronchospastic disease by Bradford.[18] Though pulmonary infection may complicate such disease, it is not the primary cause. Exertional dyspnea is progressive but is promptly relieved when the patient is at rest. The thorax is fixed with taxation of the accessory respiratory muscles. Asphyxia from cardiac failure is the most usual form of death. During the day when the patient is usually dyspneic, the usual bronchial dilators employed in asthmatic disease will give relief. As opposed to the usual attack of bronchial asthma, these patients require no medication at night as their sleep is usually undisturbed. A warning is given that oxygen should not be used, other than with judicious caution, for emphysematous patients have increased residual air and oxygen is often contraindicated. The irritation of smoke to the asthmatic patient has been emphasized by Peters and his associate workers.[86] They state that no patient with bronchial asthma should smoke tobacco, as this induces cough, bronchitis and bronchial spasm which are really warnings to avoid or expel the irritating effects of smoke. Negative cutaneous tests to tobacco products are no criteria that the patient with asthma can tolerate smoking. It has been long recognized that tobacco is a source of bronchial irritation with subsequent cough and a prolongation of the asthmatic symptoms. These authors state that the best possible regimen for the relief of chronic asthma will fail if the patient is allowed to continue the use of tobacco in any form. The challenge of emphysema is one that has been answered by very few investigators. Smart, Davenport and Pearson[106] treated their patients with 100 per cent oxygen and aerosols of various medication. They used the intermittent positive pressure breathing with the Bennett pressure-therapy unit. Isuprel, Aerolone compound, and Vaponephrin were three potent broncho-dilators used with

about equal success. These medications were given by nebulization with a control pressure of 20 cm of water. At the beginning of therapy, many patients have a tendency to hyper-ventilate. Mild tetany was noted on a few occasions. Treatments were given for about twenty minutes three times daily for about three weeks or for as long as the patient continued to show progressive improvement either by actual measurement or by symptomatic relief. These investigators feel that pressure breathing is the most effective therapy to be used in the management of early or moderately advanced emphysema. Positive pressure breathing becomes largely palliative therapy in the end stages of the disease where there is marked loss of alveolar elasticity. Breathing exercises in the therapy of bronchial asthma have been described by Nelson.[80] Little excursion of the thorax occurs in the usual attack of bronchial asthma. The average asthmatic attack is initiated with a generalized spasm of the smooth muscle in the finer bronchioles, followed by edema of the mucosa and an accumulation of secretion. The objectives of breathing exercises for the asthmatic patient are listed by Nelson as follows: (1) to re-educate the patient to use his diaphragm more effectively in quiet respiration, (2) to increase vital capacity, (3) to restore the enlarged chest to proportions as nearly normal as possible and to prevent enlargement of the chest, (4) to abort asthmatic attacks. Nelson advises the asthmatic patients to lie on their backs with head and knees comfortably supported by pillows. They then should breathe through their noses and exhale slowly through their mouths making an "f" or "s" sound. This should be repeated at least three times. They should also learn to keep the upper part of the chest still during inhalation so that inspiration is carried out mainly by the diaphragm. The patients are advised to sit in a chair with a wide belt (at least five inches in width) around their lower ribs, above their waists. They hold to the end of this belt, breathing out slowly, sinking first the upper chest, then the ribs and finally compressing the ribs by tightening the belt. These exercises tend to stress contraction of the diaphragm and increase the expiratory phase of respiration.

DERMATOLOGY

Because itching is a function of the epidermis, this complaint is not present when this part of the skin is denuded. Pain and itching are closely related so that the itch sensation in many cases is only a forerunner of pain. Nerve fibres for itch are carried from the skin to the spinal cord in peripheral nerves traveling up the spinal thalamic tracts to the thalamus and the cortex. Because of the close relationship between itch and pain, scratching relieves the itch by stimulating the pain endings and by injuring the skin. This converts the sensation of itch to that of pain. Lichenification is the term applied to the resultant protective thickening of the skin. This predisposes to more itch because the involved area is more dry with plugged sweat and duct pores. Because dry skin will always itch, exogenous hydration is advisable. Lobitz and Jillson[73] advise the use of occlusive dressings or the application of any hydroprobic substance (such as petrolatum) because this complements hydration. Topically applied local anesthetic agents are not absorbed into the intact skin in any amount to alter itch or pain sensation. Upon this basis, therefore, they consider antihistamine drugs to be of no value in relieving itch when applied locally. They cannot penetrate the intact skin. If antihistamines are to be used for the relief of the itch sensation they

should be taken by mouth; and then be used only for the itch produced by histamine—as compared to the nonhistamine produced itch of poison ivy dermatitis. Aspirin decreases itch and is very effective in this systemic approach. These authors list diabetes, hepatic disease, kidney disease, blood dyscrasias, pregnancy and psychiatric disorders as being predominant among the internal causes for itching. In each instance of itch, which in itself is only a symptom, individual measures of therapy must be employed. They are directed at the underlying cause if this is known or can be recognized. In answer to a questionnaire sent out by Ellis and Bundick,[39] 200 dermatologists reported their experience with topical antihistamines. Ninety-four per cent of these men had tried the topical use of antihistamines, but only 60 per cent were still using them. Less than 10 per cent prescribed them with any degree of regularity or frequency. These preparations were discontinued primarily because they were thought to be ineffective, tended to aggravate the dermatoses under treatment, or resulted in too high an incidence of contact type sensitization. Thephorin ointment caused the highest number of instances of contact dermatitis. The frequency of reactions seemed to increase as the popularity of the medication increased, indicating a close correlation between those antihistamines causing contact dermatitis and those considered to be most valuable.

Therapeutic dermatitis is due to sensitivity either inherited or acquired far more often than it is to simple irritation. This has been the experience of Lane.[68] The most common sensitizers in this gentleman's experience have been local anesthetics, sulfonamides, penicillin, mercury, phenol, tar, menthol, camphor, nitrofurazone, iodine, and salicylic acid. Acute conditions of the skin are more easily exacerbated by local applications than are chronic states. He advises the use of careful questioning as to previous disease, therapy and results before any application is made to the diseased skin. In this way physicians may prevent therapeutic reactions by their applications. Because about 10 per cent of sensitized persons will have a generalized dermatitis, hospital care is often needed and convalescence may be long and stormy. This of course adds to the seriousness of the situation. Of special interest is a case reported by Jordon.[65] Dermatitis venenata was noted from local contact with isonicotinic acid hydrazid. Because of the use of this drug in the treatment of tuberculosis, professional people who handle the drug (pharmacists, physicians, nurses or patients) may develop a cutaneous sensitivity from local contact. It should be suspected in those persons as a cause of any unexplained dermatitis venenata that may appear. Because many cases of allergic dermatoses due to drugs are still unrecognized by the patient and undiagnosed by the physician, any current statistical survey of the incidence falls far short of the true figure. Sulzberger and Witten[114] feel that both mild and serious reactions are due to allergy to drugs rather than to their toxic and poisonous actions. Not all untoward manifestations following the use of drugs are allergic in nature. Some are due to still unknown processes, some to combinations of allergic and nonallergic mechanisms, some to primarily toxic effects and some to the shift in ecologic influences through destruction of the drug-sensitive microorganisms. They describe three periods which are characteristic of immunologic sensitization: the period of refractoriness to sensitization, the period of incubation, and the reaction time or latent period. It is extremely important to recognize the dermatosis as one presenting

characteristics which should direct suspicion to certain drugs. The history of the actual exposure to the suspected drug is of primary importance. They cite the danger of recurrence or exacerbation on re-exposure to the suspected or known cause of the dermatitis. The attention of the physician to the increasing number of instances of therapeutic contact dermatitis has been reported by Nomland.[81] He describes several typical cases of sensitivity and emphasizes the value of the patch test in making a definite diagnosis of cause. He gives the additional information that medications which may subsequently be given internally should not be used in topical treatment because of the potential dangers of combined sensitivity to these drugs. O'Leary[82] emphasizes that the use of cortisone and corticotropin in most diseases of the skin is of short duration. The pruritus of atopic eczema, dermatitis herpetiformis, acute urticaria, pruritus ani, pruritus vulvae and neuro-dermatitis can be minimized by the use of cortisone. These benefits, however, are not constant and are short lived. Though the anaphylactic reaction of penicillin sensitivity may continue, these hormonal ointments may minimize or eradicate the urticarial lesions. Recurrence of lesions of pemphigus, scleroderma, atopic eczema, and sarcoidosis is noted on cessation of treatment. He advises that both cortisone and corticotropin be administered with caution and discretion when used locally on the skin. Sternberg and his associates[112] believe that the use of cortisone in atopic dermatitis should be confined to severe cases when all other conventional forms of therapy have failed to arrest the progress of the disease. So strong are they in this belief that they consider cortisone therapy to be contra-indicated in mild to moderate cases of atopic dermatitis. Contact dermatitis due to pork corticotropin has been reported by Zeligman.[130] His patient completely cleared after she had stopped handling corticotropin for one month. At the end of this time she was again instructed to handle corticotropin and within two days had a recurrence of eyelid dermatitis and a scaling itching dermatitis on the dorsal surfaces of both index fingers. Patch testing with pork corticotropin gave large reactions on two occasions as compared with negative reactions with beef corticotropin. Goldman[52] was able to produce a definite inhibiting effect on both the immediate and late reactions to mosquito bites. This was done with the injection of compound S with the inhibitory effect persisting for at least four mouths in some instances.

At a recent dermatology postgraduate session the question was raised for a panel discussion on the treatment of hand dermatitis. Surprisingly, the statement was made that if this subject were opened, the remaining part of the program would be of little or no importance—so deep was the interest and so complicated was the problem. Cormia[28] has stated that perhaps the most confusing syndrome encountered in dermatology is that of hand dermatitis. Contact dermatitis was by far the most common cause in 150 cases of hand eczema seen by this author. Second in importance was that of dermatophytid. Food allergy, localized atopic eczema, vesicular neuro-dermatitis, numular eczema and others were of lesser importance. Irritation, infection, over-treatment, heat, food allergy and endocrine problems were given as secondary factors contributing to the development, relapse or persistence of the eruption. It has been emphasized that all cases of hand dermatitis should be carefully investigated and the causative factors identified and eliminated. This is certainly a difficult problem for the average man in dermatology or allergy. In contact dermatitis of the hand, the location of the lesion is often confined sharply to the actual area

of contact. The use of elimination diets to substantiate a diagnosis of food allergy has been mentioned. If food allergy is a basis for the hand lesions, these then may resemble eruptions of dermatophytosis or vesicular neuro-dermatitis. Baer and Ludwig[5] agree with this former author. They state that eczema of the hands is one of the most difficult cutaneous eruptions to manage. Because primary irritants may complicate the picture, no clinical appearance is absolutely pathogonomic for a particular type of eczematous eruption. The sole factor in contact dermatitis, "id" eruptions, drug eruptions and food sensitivity reactions is that of allergy. In making a diagnosis of cause, these authors stress the importance of a thorough and complete history. The palms of the hands are usually more resistant to the action of various irritants and allergens than are other sections of the skin. Exogenous contamination and hemotogenous spread may account for the jumping or skipping of eczema. In contrast to some men, Baer and Ludwig feel that hand eczema caused by food sensitivity is rather a rare finding. Skin tests are useless as an investigative measure. They depend more upon elimination diets, food diaries or starvation routines as attempts to determine the cause. The care of the patient with hand dermatitis is a problem filled with diagnostic and therapeutic hazards as evidenced by the "shopping around" that the patient with these complaints will do. That food allergy is an important cause of eczematous dermatitis of the hand is described by Flood.[45] It is impossible to make a diagnosis of food allergy by inspection of the hands alone. The primary lesion of the disease is a vesicle which seems to appear in crops and is usually deep seated. These patients usually have had their dermatitis for a long period of time and have made the rounds from general practitioner to dermatologist to allergist. Usually they have had their tolerance of roentgen therapy. If there is no active fungus infection demonstrable on the hands or feet, if there are no obvious contact factors and if the recurrent vesicular eruption has been of six months or many years' duration, then food allergy should be suspected as a cause. Flood uses a basic diet consisting of beef, salmon, cabbage, Ry-Krisp, cherries, pears, prunes, tea, salt and sugar. One of the most important requirements in food allergy of the hands is to have the patient co-operate to the best of his ability. Flood states that 20 per cent of hand dermatitis cases will find the cause of their complaints in food allergy.

The management of fungus infections will be more exact when the broad clinical characteristics of the individual fungi are recognized. Lewis, Dougherty and Standish[71] offer a practical classification as follows: 1. microsporum, 2. trichophyton, 3. epidermophyton and 4. monilia. The microsporum produce tinea capitis and tinea corporis. With *M. audouini* the intracutaneous test with trichophyton may or may not be positive. With *M. lanosum,* however, the intracutaneous trichophyton test is invariably positive. *Trichophyton gypseum* causes athletes foot in which all stages of inflammation may be seen. The allergic response to this organism is marked, but negative trichophyton reactions are exhibited on skin testing with trichophyton schoenleimi. This latter is the cause of favus. The manifestations of *Candida* (monilia) *albicans* may be cutaneous or systemic. Skin testing for oidiomycin sensitivity is of no practical value in establishing a diagnosis.

Urticaria is only a symptom. Rostenberg and Harris[96] reveal the various causes of this symptom to be allergic or nonallergic in origin. Acute urticaria usually will be based on exogenous causes while chronic lesions

are more apt to be founded upon endogenous sources. Foods and drugs are the most common ingestants causing urticaria lesions. Inhalant substances should not be overlooked. Though heat and cold have been reported as causally responsible for urticaria, many so-called physical allergies are inappropriately designated. There is no established evidence to support this latter feature as a true sensitization mechanism. Toxic materials liberated by micro-organisms account for acute urticaria due to endogenous substances. These authors put little faith in a diagnosis of focus of infection. In all chronic cases of urticaria a thorough search should be made for parasites. They are a relatively common cause for hives. Psychogenic stimuli as sole causal factors in urticaria have not been adequately proven in the experience of these authors. In treatment, antihistamines perform their most useful function in acting as barriers between the reacting tissue and the antigen-antibody union. Epinephrine has little place in the therapy of urticaria and hormonal agents are not indicated in the usual instance.

INFECTION

The concept of focal infection has become an accepted principle in the practice of medicine according to Coleman.[27] He describes four ways in which foci of infection may initiate or effect the course of a disease or malady. Bacteria may be discharged from the focus onto a free surface and the disease may be extended by re-inoculation. Bacteria may be carried to distant parts of the body by the lymphatics or by the hematogenous route. Lymphadenitis or abcess formation may occur when this infection is arrested by the lymph nodes. As a result of bacterial metabolism, products of such procedures may reach or damage remote parts of the body. Bacteria at the focus may undergo dissolution with these products diffusing into the blood or lymph streams sensitizing various tissues of the body in an allergic sense. Because of this original sensitization, later liberation of dissolution products may result in an allergic reaction. General debility, fatigue, malaise, anorexia, headache, drowsiness, anemia, loss of weight, hypotension and reduced immunological responses are some of the results of focal infection. The reluctance of many allergists to acknowledge the theory of infective allergy has greatly hampered this specialty in general. Chobot[24] hopes that more physicians will recognize the necessity of removing these foci as a part of their therapeutic program. The average physician in allergy will then begin to understand the importance of bacterial sensitivity. He states that bacterial invasion is responsible for such diseases as erysipelas, rheumatic fever, tuberculosis and syphilis. Because bacteria give delayed reactions of tuberculin type instead of an immediate wheal reaction, diagnosis of bacterial allergy has always been a difficult problem. Since there is no relationship between a skin reaction and an active infection, skin tests with bacteria have been without value. In opposition to this is the reproduction of an allergic picture with an injection of autogenous vaccine. This represents the only accurate indication of bacterial allergy in adults. In children the most frequent foci are found in the tonsils and adenoids. This author stresses the importance of infection in diseases of the skin, particularly eczema and urticaria. He has reported that infection is the most important single cause of asthma in children, with 30 per cent of 400 patients having infectious asthma. Those asthmatic patients who do not receive benefit from hospitalization or food allergen elimination usually have disease of bacterial origin. The

importance of associated asthma and acute head and chest colds has been mentioned, but the author states that this one finding may be somewhat misleading. In the adult patient, sinus and dental infection are the usual allergic causes. The infected sinus tissue must be removed as completely as possible, once sinus disease has been established as a diagnosis. He does not recommend sinus surgery in adult patients over fifty years of age, in those who have had asthma for five years or more, nor in those with marked emphysema and other irreversible changes in the chest.

HEADACHE

Proper analysis of head pain necessitates a detailed history, physical and neurologic examination and thorough investigation of the individual's personality and present life situation. Meriwether, Culpepper and Tuthill[77] state that the history of headache patients must consider the circumstances relative to the onset, previous diagnostic studies and efficacy of therapy that has been employed. They class migraine, histaminic cephalgia, atypical vascular headache, hypertension, temporal arteritis, aneurysms, and vessel occlusion as vascular conditions causing head pain. They question whether migraine and histaminic cephalgia are merely different reactions to a basic underlying cause. A patient with psychosomatic disturbances and considerable nervous tension is usually the one that has atypical vascular headaches. The general classification of headache and the comment upon each group are highly recommended as review material for anyone interested in this entrancing problem. Importance of psychogenic factors in the pathogenesis of migraine and tension headaches has been described by Krupp and Friedman.[67] Initial vaso-constriction of cerebral arteries produces the pre-headache phenomenon of migraine. The absence of abdominal disorders in association with childhood migraine is a point worthy of note. Most children with migraine, according to these writers, will have psychogenic symptoms of nail-biting, thumb-sucking and enuresis. Psychotherapy has been suggested in most cases, particularly when the neurotic symptoms are outstanding and the headaches are severe and frequent. Ergotamine tartrate and caffeine are recommended for treatment. The importance of administration in the prodromal phase of the headache has been emphasized by the authors. That childhood migraine seldom reaches the stage of obstinate chronicity has been mentioned by Michael and Williams.[78] Though they cannot assign any definite etiology to childhood migraine, the usual factors of allergy, heredity and previous concussion show a predominance in most cases. They mention the importance of recognizing familial trends in these headaches. Of twenty cases studied, electroencephalographic studies were normal in only one patient. Of the entire group, only two children had allergic manifestations co-existent with migraine. Hilsinger[58] studied twenty-five patients with complaints of vascular headaches. He employed Bellergal with the dosage of the drug adjusted to the individual needs of each patient. They found that the drug dampened the effect of the undesirable nerve impulses to the autonomic nervous system. The use of this preparation, Bellergal, was also described by Wittich.[128] Through the action of the three components of Bellergal—ergotamine tartrate, Bellafoline and phenobarbital—an inhibitory action is exerted on the three divisions of the neuro-vegetative system. This author describes six cases in whom the preparation was used. The dosage was individualized for each patient with the maintenance dosage being continued for three out of

each four weeks. His patients represented mostly allergic patients who had a low tolerance to the more commonly used vaso-constrictors.

The effective treatment of migraine continues to be a major problem, particularly in the patient who fails to respond to the usual forms of therapy. Zanfagna[129] has employed rectal suppositories of ergotamine tartrate-caffeine with reportedly good results. Thirty patients were studied in this presentation. All patients were given rectal suppositories containing 2 mg of ergotamine tartrate and 100 mg of caffeine. Original instructions suggested the use of the suppository within one hour of the onset of the headache. A group of patients were advised to use the suppositories one to two hours after the onset of the headache and in a third section, patients were asked to wait three hours after the onset before using the rectal inserts. Excellent results were reported in twenty-four patients when the rectal medication was used within one hour of the onset of the distress. These excellent results decreased in frequency with the lengthening of time between the onset of the headache and the use of the material. Only six of the thirty patients complained of an aggravation of nausea and vomiting accompanying the headache. Perhaps the best advantage of the rectal use of ergotamine tartrate in this form would be in the patient unable to retain anything taken by mouth. The importance of distinguishing migraine from other headaches in order that a good therapeutic result may be assured is a point well taken by Friedman and his associates.[47] The basic factors that cause dilatation and which alter the sensitivity of the blood vessel and its periarterial plexus are not definitely known. These authors list several concepts for the production of such findings. They range from metabolic disturbances and allergy to heredity and endocrine factors. These workers feel that the mechanism of headache in all cases of migraine is peripheral, involving the stimulation of pain endings as a result of vascular changes. On the basis of changes in the cerebral and meningeal circulation the prodromae, course, symptoms, signs and sequelae of the disorder are explained. Initial vaso-constriction of the cerebral arteries produces the visual and other pre-headache phenomena. A subsequent dilatation and distention of the cranial arteries in the distribution of the external carotid causes the pain. Various criteria for diagnosis consist of a recurrent headache, with temporal visual disorders, associated with nausea and vomiting, in a person with characteristics of perfectionism and rigidity. Therapeutic trial with relief by ergotamine derivatives can be used to rule out other forms of headache. Tumors, trauma, endocrine disorders, systemic findings, neuralgias, tensional headaches, and others are types of headache which must be differentiated from so-called true migraine. These authors list peripheral vascular diseases, hypertension, coronary disease and impaired liver function as being the main features contra-indicating the use of ergotamine medication. Intensive deep level psychotherapy has been recommended as a part of better migraine therapy. The importance of psychotherapy as an adjunct in migraine has been introduced by von Witzleben.[120] If there are no underlying organic lesions, most migraine patients, according to this writer, will respond to psychotherapy. He feels that migraine is a psychosomatic problem. Drug therapy will not replace or even act as a substitute for this measure, but may be used with judicious care when contact with a psychiatrist is not possible. This preliminary report, in the opinion of this reviewer, is too biased and does not give freedom of thought and expression in the management of this particular problem.

Sooner or later I knew someone would do it! Cortisone in allergic migraine has been reported by Blumenthal.[15] His single patient received 200 mg of cortisone for two days and then 100 mg a day for one week. The headaches were completely eliminated for a period of three weeks and thereafter recurred following cessation of cortisone treatment. Maintenance dosage of 25 mg twice daily seemed to be satisfactory. There were no side effects from the use of the preparation. This reviewer can see no basis for the use of cortisone in allergic migraine when the condition is admittedly one of recurrent attacks dependent upon so many and varied causes with influencing factors.

That migraine has no hereditary relationship with bronchial asthma was the subject of an investigation by Schwartz.[100] He found a total of 171 patients with migraine among 3,815 interviewed. Most of these ascribed the cause of their headaches to nervousness, worries or strenuous mental work. Not one of the patients with headache gave a history of exogenous factors of probable allergic nature. On the other hand, 80 per cent of fifty-five patients with classical migraine were either completely or almost completely relieved of attacks by detection and elimination of the causative foods. Unger and Unger[119] review the problem of migraine headaches and find that allergy to foods is the prime precipitating cause of this condition. Chocolate was given as the most common cause of migraine, but most patients sensitive to it find it out for themselves. This finding is never determined by doing skin tests. These authors admit that psychic factors are important in migraine and though they are not the prime factor, they may be the most obvious. Because they reveal the most of the minor causes of frequent attacks, food diaries are an important part in the diagnostic ritual. Once the causative substance or substances have been determined, the prevention of attacks gives the patient a wonderful sense of security. Complete relief for 60 per cent of fifty-five patients was found by avoiding causative foods and following a rather strict elimination diet. Another 20 per cent had been partially relieved, while over 84 per cent found relief to be from 75 per cent to 100 per cent. Intravenous calcium as a recent addition to the therapy of migraine attacks has been emphasized by these authors.

Davison[31] presents a very enlightening article on allergy of the nervous system in which he produces evidence that allergic sensitivity not infrequently causes symptoms referable to the nervous system. He makes reference to reports of ninety-two patients with epilepsy whose attacks were completely relieved by allergic management without the use of anticonvulsives. Since this is in direct opposition to notes previously made in this review, it is recommended that all interested individuals review this carefully written article with its large bibliography.

BIBLIOGRAPHY

1. Ambrus, J. L.; Ambrus, C. M., and Harrisson, J. W. E.: Mode of action of histamine desensitization. Am. J. Physiol., 167:268, 1951.
2. Anderson, J. R.: Letters of Inter. Corr. Soc. Series 15, page 86.
3. Answers to Questionnaire: Letters of Inter. Corr. Soc. Series 15, pages 86-88.
4. Answers to Questionnaire: Letters of Inter. Corr. Soc. Series 15, pages 144-149.
5. Baer, R., and Ludwig, J. S.: Allergic dermatitis of the hands. Post-Grad. M. J., 12:41 (July) 1952.
6. Baird, K. A.: Letters of Inter. Corr. Soc. Series 15, page 10.

7. Baker, Harry: Differential diagnosis of convulsions in children. Bull. Vancouver M. A., 28:119, 1952.
8. Baldwin, H. S.: The place of the allergist in medical education and public welfare. Ann. Allergy, 10.422 (July-Aug.) 1952.
9. Bentolila, L., Vila Ortiz, J. M., and Bertotto, E. V.: Allergic cataract. Ann. Allergy, 10:36 (Mar.-Apr.) 1952.
10. Berdal, P.: Serologic investigations on the edema fluid from nasal polyps. J. Allergy, 23:11 (Jan.) 1952.
11. Berley, B. S., and Saland, G.: Febrile hypersensitivity to quinidine given orally. J.A.M.A., 148:1121 (Mar. 29) 1952.
12. Bernton, H. S.: Letters of Inter. Corr. Soc. Series 15, page 9.
13. Bernton, H. S.: Food allergy with special reference to corn and refined corn derivatives. Ann. Int. Med., 36:177 (Jan.) 1952.
14. Bluefarb, S. M., and Steinberg, H. S.: Pulmonary manifestations of mycosis fungoides. Ann. Int. Med., 36:625 (Feb.) 1952.
15. Blumenthal, J. S.: Cortisone in allergic migraine. Minnesota Med., 35:209 (Mar.) 1952.
16. Blumstein, G. I., and Johnson, J.: Gastrointestinal allergy simulating regional enteritis. J.A.M.A., 147:1441, 1951.
17. Bowen, Ralph: Letters of Inter. Corr. Soc. Series 15, page 48.
18. Bradford, J.: Progressive bronchospastic disease. Am. Prac., 3:349, 1952.
19. Brown, E. A.: The field of allergy. J. Kansas Med. Soc. (Feb.) 1952.
20. Brown, E. A.: Standardization of allergens. Premier Congres International D'Allergie, Zurich, Sept. 1951.
21. Cazort, Alan: Letters of Inter. Corr. Soc. Series 15, page 2.
22. Cazort, Alan: Letters of Inter. Corr. Soc. Series 15, page 150.
23. Chitwood, W. R., and Moore, C. D.: Anaphylactic shock following intravenous administration of vitamin B complex. J.A.M.A., 148:461, 1952.
24. Chobot, R.: Infectious factors in pediatric and adult allergy. J.A.M.A., 150: 1480 (Dec. 13) 1952.
25. Clark, H. G.: Letters of Inter. Corr. Soc. Series 15, page 3.
26. Code, C. F.: Histamine in the blood. Physiol. Rev., 32:47, 1952.
27. Coleman, G. H.: Present status of concept of focal infection. J.A.M.A., 151: 280 (Jan. 24) 1953.
28. Cormia, F. E.: Eczema of the hands. Canad. M.A.J., 66:451, 1952.
29. Crandall, F. G.: Practical concepts of allergy. Ann. West. Med. & Surg., p. 567 (Sept.) 1952.
30. Crandall, F. G.: Public relations in the practice of allergy. California Med., 76:158 (Mar.) 1952.
31. Davison, H. M.: Allergy of the nervous system. Quart. Review of Allergy and Applied Immun., 6:157 (June) 1952.
32. de la Riva, G. Estrada: Variaciones en la micologia ambiental de Cuba. Inter. Arch. Allergy and Applied Immun., 2:362, 1951.
33. Derkacki, E. L.: Aural manifestations of allergy. Ann. Otol., Rhin. & Laryng., 61:179, 1952.
34. Diaz, C. J.; Albert, C.; Barrantes, V. L.; Lahoz, F.; Salgado, L., and Lahoz, C.: New roentgenographic technique in bronchial asthma. J.A.M.A. 150: 1297 (Nov. 29) 1952.
35. Dolger, Henry: The management of insulin allergy and insulin resistance in diabetes mellitus. M. Clin. North America, 36:783 (May) 1952.
36. Editorial: J. Allergy, 23.478 (Sept.) 1952.
37. Editorial: Ann. Allergy, 10:487 (July-Aug.) 1952.
38. Editorial: J. Allergy, 23:558 (Nov.) 1952.
39. Ellis, F. A., and Bundick, W. R.: Appraisal of topical use of antihistamines. J.A.M.A., 150:773 (Oct. 25) 1952.
40. Fabricant, N.: Effect of progressively buffered solution of ephedrine on nasal mucosa. J.A.M.A., 151:21 (Jan. 3) 1953.
41. Feinberg, S.: Drug allergy—Some chemical and immunological aspects. Ann. Allergy, 10:260 (May-June) 1952.
42. Feinberg, S. M.; Feinberg, A. R., and Bigg, E.: Allergy to pituitary corticotropic hormone. J.A.M.A., 147:40, 1951.
43. Ferris, H. E.; Alpert, S., and Coakley, C. A.: Prevention of allergic transfusion reactions: The prophylactic use of antihistamine in blood to prevent allergic transfusion reactions. Am. Pract., 3:177, 1952.
44. Finke, W.: Childhood pneumonia, a common cause of broncho-pulmonary disease. Am. J. Dis. Child., 83:755 (June) 1952.

45. Flood, J. M.: Eczematous dermatitis of the hands due to food allergy. Post-Grad. M. J., 13:26 (Jan.) 1953.
46. Friedewald, V. E.: Is skin testing in allergic patients worth the effort? J. Allergy, 23:420 (Sept.) 1952.
47. Friedman, A. P.; Karron, I., and Pool, N.: Migraine. Post-Grad. M. J., 11:33 (Jan.) 1952.
48. Friedmann, R. A.: Chemical and immunological properties of timothy grass pollen extracts and the problems of standardization. Quart. Review of Allergy and Applied Immun., 6:290 (Sept.) 1952.
49. Fries, J. H.: Roentgen studies of allergic children with disturbances of the pylorus resulting from food sensitivity.. J. Allergy, 23:39 (Jan.) 1952.
50. Gilbert, F. I., Jr., and Arnold, H. L., Jr.: Failure of corticotropin to prevent acute hemolytic anemia due to sulfapyridine. J.A.M.A., 150:95 (Sept. 13) 1952.
51. Goldman, L., and Rockwell, E.: Summary of Exhibit. Amer. Acad. of Derm. and Syph., Chicago, Ill., 1951.
52. Goldman, L.: Local effect of compound F on reactions to mosquito bites. J.A.M.A., 149:265 (May 17) 1952.
53. Grollman, Arthur: The use and abuse of drug therapy. J. Omaha Mid-west Clin. Soc., 13:75 (Aug.) 1952.
54. Hansel, F. K.: Methods of immunization employed in the treatment of sinusitis. Ann. Allergy, 10:131 (Mar.-Apr.) 1952.
55. Harkness, G.: Maxillary sinusitis. J. Iowa M. Soc., 42:571 (Dec.) 1952.
56. Harms, H. E., and Saniat, T. L. L.: The meaning of fatigue. Med. Clin. North America, 36:311 (Mar.) 1952.
57. Hellman, E.: Allergy to procaine amide. J.A.M.A., 149:1393 (Aug.) 1952.
58. Hilsinger, R. L.: Headache and autonomic imbalance. Laryngoscope, 61:296 (Apr.) 1951.
59. Jaros, S. H.; Wnuck, A. L., and deBeer, E. J.: Thiamine intolerance. Ann. of Allergy, 10:291, 1952.
60. Jeans, P. C.: Quoted in Editorial, J.A.M.A., 148:1126 (Mar. 29) 1952.
61. Johnston, C. R. K.: Chemical agents unsuccessfully employed as substitutes for ACTH and Cortisone. Ann. of Allergy, 10:197 (Mar.-Apr.) 1952.
62. Jonez, H. D.: Management of multiple sclerosis. Post-Grad. M. J., 11:415 (May) 1952.
63. Jonez, H. D.: The use of histamine in the treatment of allergic diseases. Ann. Allergy, 10:454 (July-Aug.) 1952.
64. Jonez, H. D.: Repository histamine therapy in allergy. Quart. Review Allergy and App. Immun., 6:283 (Sept.) 1952.
65. Jordon, J. W.: Cutaneous allergy from local contact with isonicotinic acid hydrazid. J.A.M.A., 149:1316 (Aug. 2) 1952.
66. Kaufman, William: Self-inflicted, food-induced allergic illness. Ann. Allergy, 10:308, 1952.
67. Krupp. G. R., and Friedman, A. P.: Recurrent headache in children: a study of 100 clinic cases. New York State J. Med., 53:43, 1953.
68. Lane, C. G.: Therapeutic dermatitis. New England J. Med., 246:77, 1952.
69. Letters to the Editor: J.A.M.A., 150:1512 (Dec. 13) 1952.
70. Letters to the Editor: J.A.M.A., 150:1512 (Dec. 13) 1952.
71. Lewis, G. M.; Dougherty, J. W., and Standish, E. M.: Superficial fungous infections. Post-Grad. M. J. 12:27 (July) 1952.
72. Little J. G.: Letters of Inter. Corr. Soc., Series 15, page 3.
73. Lobitz, W. S., Jr., and Jillson, O. F.: The physiologic approach to the management of itching. Post-Grad. M. J. 12:2 (July) 1952.
74. McGuinness A. C.: Immunization procedures in private practice. M. Clin. North America, 36:1599 (Nov.) 1952.
75. McKay, C. R.: Failure of antihistamines in severe sulfadiazine hypersensitivity. Rocky Mountain M. J., 49:441, 1952.
76. MacLaren, W. R.: Letters of Inter. Corr. Soc., Series 15, page 27.
77. Meriwether, L. S.; Culpepper, W. S., and Tuthill, S. W.: Headache, syncope and vertigo. M. Clin. North America 36:319 (Mar.) 1952.
78. Michael, M. L., and Williams, J. M.: Migraine in children. J. Pediat., 41: 18, 1952.
79. Miller, A. R.: Nasal triad, nasal allergy and deafness. Northwest. Med., 51:302, 1952.
80. Nelson, P. A.: The therapeutic basis of breathing exercises. Cleveland Clin. Quart., 20:269 (Jan.) 1953.

81. Nomland, R.: Therapeutic contact dermatitis. J. Iowa M. Soc., 53:150 (Apr.) 1953.
82. O'Leary, P. A.: Cortisone and corticotropin in the treatment of cutaneous diseases. Post-Grad. M. J., 12:10 (July) 1952.
83. Orie, N. G. M.: Candida (monilia) infection of the respiratory tract. Dis. of Chest, 22:107 (July) 1952.
84. Overholdt, R. H.; Walker, J. H., and Woods, F. M.: Hidden or unsuspected bronchiectasis in the asthmatic patient. J.A.M.A., 150:438 (Oct.) 1952.
85. Pepys, J., and Duveen, G. E.: Negative skin tests in allergic rhinitis and nasal polyposis. Inter. Arch. Allergy and Applied Immun., 2:147, 1951.
86. Peters, G. A.; Prickman, L. E.; Loelsche, G. A., and Carryer, H. M.: Smoking and asthma. Proc. Staff Meet. Mayo Clin., 27:329 (Aug. 13) 1952.
87. Queries and Minor Notes: J.A.M.A., 151:1052 (Mar. 20) 1953.
88. Queries and Minor Notes: J.A.M.A., 149:1360 (Aug. 2) 1952.
89. Ratner, Bret, and Silberman, D. E.: Allergy—its distribution and the heredity concept. Ann. Allergy, 9:1 (Jan.-Feb.) 1952.
90. Ratner, Bret: Pathogenesis of allergy in infancy and childhood. Bull. New York M. Coll., 14:54, 1951.
91. Ratner, B.; Untracht, S., and Collins-Williams, C.: Allergencity of modified and processed foodstuffs. I. The use of a dual ingestion passive transfer test to determine the allergenicity of foodstuffs in man. Ann. Allergy, 10: 675 (Nov.-Dec.) 1952.
92. Rawlins, A. G.: Hormonal-connective tissue mechanism in allergy. Ann. Allergy, 10:440 (July-Aug.) 1952.
93. Reisner, E. H.: Hematologic manifestations of an allergic nature. J. Allergy, 23:550 (Nov.) 1952.
94. Rinkel, H. J.; Randolph, T. G., and Zellers, M.: Food Allergy. Springfield, Ill.: Charles C Thomas, 1951.
95. Rinkel, H. J.: Thermal allergy. Clinical evaluation and management. South. M. J., 44:1067, 1951,
96. Rostenberg, A., Jr., and Harriss, H. E.: Causes and treatment of urticaria. Post-Grad. M. J., 12:52, (July) 1952.
97. Ruzic, J. P.; Dorsey, J. M.; Huber, H. L., and Armstrong, S. H., Jr.: Gastric lesion of Loeffler's syndrome. J.A.M.A., 149:534, 1952.
98. Samter, M., and Kofoed, M. A.: On the rationale of treating allergic diseases with bacterial pyrogens. J. Allergy, 23:327 (July) 1952.
99. Schuman, C., and Simmons, H. G.: Cardiac asthma: Its pathogenesis and response to aminophylline. Ann. Int. Med., 36:864 (Mar.) 1952.
100. Schwartz, M.: Is migraine an allergic disease? J. Allergy, 23:426 (Sept.) 1952.
101. Segal, M. S., and Herschfus, J. A.: Oxygen therapy: description of a new face tent. Bull. New England M. Center, 13:244 (Dec.) 1951.
102. Sheldon, J. M.; Mathews, K. P., and Lovell, R. G.: Skin tests in atopic disease. J.A.M.A., 151:785 (Mar. 7) 1953.
103. Siegel, S. C.: Drugs used in pediatric allergy. Post-Grad. M. J., 12:563 (Dec.) 1952.
104. Siegel, S. C.; Goldstein, J.; Sawyer, W. A., and Glaser, J.: The incidence of allergy in persons who have many colds. Ann. Allergy, 10:24 (Jan.-Feb.) 1952.
105. Simon, F. A.: Letters of Inter. Corr. Soc., Series 15, page 136.
106. Smart, R. H.; Davenport, C. K., and Pearson, G. W.: Intermittent positive pressure breathing in emphysema and chronic lung diseases. J.A.M.A., 150: 1385, (Dec. 6) 1952.
107. Smith, R. B.: Letters of Inter. Corr. Soc., Series 15, page 136.
108. Smythe, F. S.: Allergies in children. Post-Grad. M. J., 12:223 (Sept.) 1952.
109. Spearman, G. K.: Letters of Inter. Corr. Soc., Series 15, page 136.
110. Staffieri, D.; Bentolila, L., and Levit, L.: Hemaplegia and allergic symptoms following ingestion of certain foods. Ann. Allergy, 10:38 (Jan.-Feb.) 1952.
111. Sternberg, T. H.; Newcomer, V. D., and Linden, I. H.: Treatment of atopic dermatitis with cortisone. J.A.M.A., 148:904 (Mar. 15) 1952.
112. Stetson, C. A., Jr.: Similarities in the mechanisms determining the Arthus and Shwartzman phenomena. J. Exper. Med., 94:347, 1951.
113. Stier, R. F. E.: Letters of Inter. Corr. Soc., Series 15, page 67.
114. Sulzberger, M. and Witten, V. H.: Allergic dermatoses due to drugs. Post-Grad. M. J., 11:549 (June) 1952.

(Continued on Page 554)

In Memoriam

ROBERT R. MONTGOMERY

Robert Russell Montgomery, a Fellow of the College since 1944, died suddenly at his home in Long Beach, California, on May 2, 1953. He was the beloved husband of Beatrice McCallum Montgomery. He is also survived by a daughter, Aileen (Mrs. Richard C. Williams, Jr.), and by three sons, Roger R., of New York City, D. W. and Cameron, of Long Beach, and seven grandchildren.

Doctor Montgomery was born in Wroxeter, Ontario, Canada, in 1884. He graduated from the Niagara Falls Collegiate Institute in 1903, receiving his M.B. degree from the University of Toronto and his M.D. degree from the University of Toronto Medical School in 1910. He interned at the General Hospital, Toronto, from 1910 to 1911, and was later resident physician at the New York Eye and Ear Infirmary. He taught at the Santa Rita Clinic, Queen of Angels Hospital, in Los Angeles, from 1937 to 1942. He was a Senior Member of the Eye, Ear, Nose and Throat Society of Los Angeles County, a member of the Seaside, St. Mary's, Community, Los Angeles County and Queen of Angels Hospitals, a Fellow of the American College of Surgeons from 1927, A Fellow of the American Triological Society, and the American Laryngological, Rhinological and Otological Society. He was certified by the American Board of Otolaryngology in 1926. He contributed much through published papers and research work in his specialty. He has been in practice in Long Beach since 1920.

He was an ardent outdoor man and sportsman and had a happy, congenial nature which will cause him to be missed by his host of friends. Members of the College extend their sincere sympathy to his family.

ALBERT HENRY BRADEN

Albert Henry Braden, a Fellow of the College since its inception, died July 22, 1953, at the age of sixty-seven. Doctor Braden was born in Bernardo, Texas, October 30, 1886. He graduated from Ford's Academy in 1909 and from the University of Texas Medical Branch in 1913. He interned at the Hotel Dieu in Beaumont, Texas, and took postgraduate studies at Tulane University Medical School in 1922 and at the Mayo Clinic in 1928 and 1929. He was pathologist at St. Joseph's Hospital from 1922 to 1944, a member of the Pathology and Bacteriology teaching staff of St. Joseph's School of Nursing and of the Sacred Heart College, Houston, Texas.

Doctor Braden had practiced medicine for forty years. He originally was a pathologist and later restricted his private practice to allergy. He was a member of his county and state medical societies, the Southern Medical Association, American Academy of Allergy, International Correspondence Society of Allergists, American Society of Pathologists, Postgraduate Medical Assembly of South Texas, American Society of Clinical Pathologists, American Association for the Advancement of Science, Southwest Allergy Forum, Texas Pathological Society, Alpha Kappa Kappa medical fraternity, and a diplomate of the American Board of Pathology. He made many contributions to medical literature, including various publications not pertaining to allergy. He also made very valuable contributions to the subject of allergy.

Doctor Braden is survived by his wife, Kathleen O'Connor Braden; four sons, Dr. A. H. Braden, Jr., and the Reverend Patrick Braden, Houston; Dr. David Braden, Galveston; J. C. Braden, Austin; and a daughter, Mrs. Kathleen Eichelberger, Fairbanks, Alaska.

Those who knew him well have lost a delightful and constant friend. He was a great character and a friend of all his professional confrères. Members of the College join with his many friends in extending sincere sympathy to his family.

News Items

SOUTHWEST ALLERGY FORUM

The next annual Meeting of the Southwest Allergy Forum will be held at the Roosevelt Hotel, New Orleans, Louisiana, May 9-11, 1954. The Officers are: Henry D. Ogden, M.D., Louisiana State University School of Medicine, New Orleans, President; Vincent J. Derbes, M.D., Tulane University School of Medicine, New Orleans, Vice President; Stanley Cohen, M.D., Tulane University School of Medicine, New Orleans, Secretary; and Nicholas K. Edrington, M.D., New Orleans, Treasurer.

The program is now being arranged.. The Southwest Allergy Forum, one of the oldest regional allergy societies, is noted for its excellent, widely diversified, programs, including papers on basic research, as well as practical papers on the subject of allergy. The traditional Southern hospitality pervades the meeting from beginning to end. There is always evening entertainment with the banquet. Members as well as non-members are welcome to attend.

CHICAGO SOCIETY OF ALLERGY

The Chicago Society of Allergy announces the following newly elected officers for 1953-1954.

President—Abe L. Aaronson
116 South Michigan Avenue
Chicago, Illinois
President-Elect—Max Samter
215 N. Elmwood
Oak Park, Illinois
Secretary-Treasurer—Simon S. Rubin
504 Broadway
Gary, Indiana

ALLERGY AWARD

Dr. Charles M. Pomerat, Professor of Cytology and Director of the Tissue Culture Laboratory at the University of Texas-Medical Branch, Galveston, Texas, who was the guest speaker at the Ninth Annual Congress of the American College of Allergists, April 28, 1953, has been awarded $1,000 by the Southwest Allergy Forum for pioneering in cellular metabolism. In addition, he received the Silver Hoektoen Award for his unusual exhibit in the field of Cytology at the American Medical Association meeting in New York City in June.

NEW COLLEGE ROSTER

Questionnaires have been sent out to all members of the College for information to be published in the first College roster. This roster will be complete, and will contain much valuable information about the College since its inception.

A large number have already returned their questionnaires. If you have any added information pertinent to this questionnaire, please send it at once to headquarters, 401 LaSalle Medical Building, Minneapolis 2, Minnesota. Those who have not yet returned their questionnaires are requested to do so immediately.

ERRATUM

On page 297 of May-June, 1953 ANNALS, the formula for children should read: Ephedrine Sulfate 12 mgm.

BOOK REVIEWS

MANUAL OF CLINICAL LABORATORY METHODS. Fourth Edition. Opal E. Hepler, Ph.D., M.D., Associate Professor of Pathology, Northwestern University Medical School, Chicago, Ill. 395 pages. Springfield: Charles C Thomas, 1953. Price $9.50.

This new fourth edition of the Manual of Clinical Laboratory Methods has been rearranged, revised and enlarged. Editorial and technical improvements have been developed as the manual was in actual use in order that it would be of maximum efficiency in the laboratory. The book is used as a standard reference by laboratory technicians and medical students when seeking explicit, step-by-step directions for the performance of laboratory tests, including their interpretation and significance. The outgrowth of this book is the result of laboratory methods prepared for use in teaching medical students in the course in clinical pathology in Northwestern University Medical School. It is not a textbook of clinical pathology, and in most instances only one method is included for each determination. The book is a guide for technicians with varying degrees of training and experience. The Manual is used both in civilian and military hospitals in many countries, and in medical schools. The illustrations and the diagrams of different types of complicated apparatus enables the technician to understand the principle upon which the particular apparatus is based and to use it with increasing assurance and accuracy.

The color plates are exceptionally well prepared. There are nineteen sections, one including allergy extracts, extracting and diluting solutions, as well as solutions used in routine testing. The print is clear and the binding one that is durable to withstand the wear of a laboratory bench.

HEREDITY IN BRONCHIAL ASTHMA. M. Schwartz, Copenhagen, Denmark. Copenhagen: Munksgaard, 1952.

This is a monograph in which the author studied the problem of inheritance of allergic diseases. He concluded that bronchial asthma is a genetic entity, and that a genetic relationship exists between asthma, vasomotor rhinitis and, probably, infantile eczema in which the specific offending allergen is clearly demonstrable. On the other hand, a large category of eczemas, urticaria, angioneurotic edema, and gastrointestinal allergy he found to be not inherited, and he separated them therefore pathogenetically from bronchial asthma. He also concluded that asthma is inherited as a Mendelian dominant with failing manifestations, so that only 40 per cent who carry the genes would ever develop symptoms.

He stated that it is not reasonable to maintain, as previous workers have done, that all allergic diseases are genetically related. In this connection, the recent studies of Ratner, Collins-Williams, and Untracht on the allergic dermal-respiratory syndrome corroborate the findings of previous workers that dermal and respiratory allergies are related, and give further evidence that there is an evolution from dermal to respiratory symptoms, and that 59 per cent of children with allergic eczema later have respiratory allergy (asthma or hay fever).

Schwartz's results are based on a statistical study of material consisting of 191 asthmatic patients, 200 controls, and 50 patients with baker's asthma. He employed the Weinberg statistical genealogical method, which he considers reliable for the demonstration of inheritance factors, if one can assume the absence of exogenous differences between the patients and the control series.

The study is included in an extensive monograph in which the author states in his introduction that there is hardly any branch of medicine in which the theories

have been so numerous, the classifications so vague, the nomenclature so divergent, and the definitions so varied. One can only be impressed with the enormous amount of time and effort expended by the author in the collection of his material and in its statistical evaluation. In discussing criteria he, too, emphasizes the lack of uniformity with regard to the material studied by previous workers, and he is of the opinion that the question of heredity in allergic diseases cannot be considered as solved and that it will remain unsolved so long as the limitation of the concept of allergy remains uncertain. With this we heartily agree. We are further impressed by the remarkable parallelism between his and our points of criticism of previous workers. We refer to the limitations of isolated pedigrees, data that are not directly comparable, undefined and sparse control material, and the controversial correlation between the age of onset and the type of family history upon which the hereditary hypothesis of Wiener, Zieve, and Fries rests.

The difficulties encountered in obtaining adequate control material is shown in Schwartz's study, in which one-half of his 200 control subjects were patients receiving ambulatory treatment at the Clinic of the National Poliomyelitis Society in Copenhagen. We shall not attempt to evaluate the influence of this type of selection, but we do not believe that it constitutes a random sample. We emphasize this because his study will stand or fall on its validity.

Schwartz divided his asthmatic patients into allergic and nonallergic groups, which corresponds with what he calls the American classification of "extrinsic" and "intrinsic," in order to ascertain whether the two groups show the same characteristics from a statistical standpoint. He concluded that the two groups are not distinguishable and that, therefore, asthma constitutes a syndrome that behaves as a genetic entity. The author concluded that urticaria, which is almost universally regarded as an allergic disease, was not inherited. It seems to us, from the data of Schwartz, that what may be inherited is not the capacity to become sensitized, but a respiratory tract that may react with the production of asthma or rhinitis due to a multiplicity of stimuli, one of which may be the antigen-antibody mechanism.

Schwartz states further that the study of baker's asthma does not permit the general conclusion that all cases of occupational asthma must be due to an inherited predisposition. In view of the fact that in 60 per cent of the bakers who suffered from asthma there was a negative family history, we feel that there is a contradiction in his conclusion that baker's asthma is inherited as a Mendelian dominant.

Other points of interest brought out by this investigator are that all persons may be sensitized, and that different occupational substances possess different capacities to sensitize. We are in accord with this, and we believe that what Schwartz was dealing with was an acquired occupational group of asthmatic persons who were exposed to an unusual concentration of a highly allergenic substance. It must be further commented upon that the sensitization period to flour that he found in his cases, averaged more than ten years. Were this due in large measure to genetic factors, such a period for the establishment of sensitization would appear inordinately long.

In a study that we made in guinea pigs on experimental asthma, we determined that quantity and certain temporal factors played an important role in the shortness of period in which the animals became sensitized. As we increased the intensity of the exposure of the guinea pigs to the inhalation of an antigenic dust, we learned that sensitization occurred earlier in direct proportion to the amount that they were exposed to. There seemed to be an optimal point, however, at which this occurred and, as the time of exposure was increased beyond this point, sensitization did not necessarily occur as early as at the optimal point.

One of the surprising things in Schwartz's extensive piece of work is that no

mention is made of the percentage of bakers who develop asthma. Do 75 per cent of bakers develop asthma, or do ten per cent develop it? It would have been interesting if Schwartz had used the bakers who had not developed asthma as controls. Under the conditions of their exposure, those who did not develop asthma would certainly have constituted an excellent control group of nonallergics.

In our guinea-pig experiment referred to above, 93 per cent of the animals developed experimental asthma. Seven per cent appeared to be resistant, the reason for which we did not determine. We concluded that our findings lend support to the belief that asthma may be regarded as an acquired condition.

Schwartz states finally that he cannot rule out the possibility that certain varieties of asthma are pathogenetically different from the spontaneous variety. We have always been at a loss to know what constitutes a spontaneous variety of asthma. Asthma is not an intrinsic disease but depends largely on exogenous factors. The antigen invading the respiratory tissues sets up a sensitization based on the antigen-antibody mechanism.

Schwartz regards Ancona's endemic asthma as a special variety of asthma to be distinguished from baker's asthma. Ancona studied a group of baker's asthma in a small Italian village, which he showed immunologically to be due to infected wheat grain and, in addition, he proved that extracts made from the particular infectious agent pediculoides and ascaris mites did induce skin reactions when injected and asthma when inhaled by these subjects. We see no difference between this form of asthma and baker's asthma due to the inhalation of flour.

Finally, Schwartz takes exception to including tropical eosinophilia and Loeffler's syndrome, which are often associated with asthma under the category of asthma, and he suggests placing them in a special group.

We are therefore critical of his establishing new sets of criteria for the various groups of antigen-antibody forms of allergy, and we believe that the sole criterion for allergy must rest on proof that the allergic syndrome is or is not initiated by an antigen-antibody mechanism.

Though the type of allergen may differ in its innate qualities for establishing allergy with greater or lesser ease, we do not believe that this would permit one to remove one or another allergen from the antigen-antibody mechanism.

One is not justified in eliminating eczema, urticaria, gastrointestinal disturbances and certain forms of asthma such as Ancona's and Loeffler's. If, in these conditions, one can elicit positive skin tests in the individual and establish a causal relation between the allergen and the syndrome through clinical test, then the condition must be accepted as allergic in character and not be arbitrarily eliminated from consideration.—B.R.

CLASSICS IN CLINICAL DERMATOLOGY. Walter B. Shelley, M.D., Ph.D., Chief, Clinic of Dermatology, University of Pennsylvania Hospital and Associate Professor of Dermatology and Syphilology, University of Pennsylvania, and John T. Crissey, M.D., Instructor, Dermatology and Syphilology, University of Pennsylvania, Philadelphia, Pa. 485 pages, 111 illustrations. Springfield: Charles C Thomas, 1953. Price $10.50.

This volume presents a nucleus of thought from which modern dermatology has grown and developed. As a source book it offers many of the ablest original contributions to the field of descriptive clinical dermatology. It draws upon ninety-five authors, twenty-one lands, and the world literature of the past century and a half. There are many full page portraits of pioneers in the field. One hundred and forty-three separate disease entities are presented in the original version of these master observers. There is a brief biographical sketch of each of the men discussed. The diseases depicted vary from those commonly seen to the unusual.

Some are case reports and others are the result of the study of many patients. The authors have carefully preserved continuity in the articles. All physicians interested in dermatology can obtain valuable information from its reading.

MÉNIÈRE'S DISEASE. American Lecture Series. Henry L. Williams, M.D., M.S. in Otol. Head of Section of Otolaryngology and Rhinology, Mayo Clinic, Professor of Otolaryngology and Rhinology Mayo Foundation, Rochester, Minnesota. 319 pages. Springfield: Charles C Thomas, 1953. Price $7.00.

The author reviews the pertinent literature concerning Ménière's disease and particularly dwells on those subjects which have seemed to produce confusion and difficulty in diagnosing the disease. He has had an opportunity to examine and treat a large number of patients with this condition and, therefore, is able to give commanding and practical information on differential diagnosis, symptoms, diagnostic tests and treatment.

Rather than stating that Ménière's disease is due to many extrinsic or intrinsic factors, this book shows how the underlying physiologic mechanism producing functional pathologic changes may be reversed by relatively simple therapeutic measures. The author discusses an improved working hypothesis for allergy so that the new classification would include physical allergy, bacterial diseases, and humoral allergy. The effect of the new hypothesis of allergy on the therapy of Ménières's disease is discussed.

This monograph, as others of the American Lecture Series, is an excellent up-to-date treatise on Ménière's disease.

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115. Swinney, B.: Letters of Inter. Corr. Soc., Series 15, page 33.
116. Szilard, Z.; Rauss, K.; Szabo, I.: New viewpoints in the pathogenesis and therapy of chronic cholecystitis. Inter. Arch. Allergy and Applied Immun., 2:160, 1951.
117. Talley, J. B.: Letters of Inter. Corr. Soc., Series 15, page 49.
118. Tuft, L.: Problems of the geriatric and their clinical management. J.A.M.A., 146:1480, 1951.
119. Unger, A. H., and Unger, L.: Migraine is an allergic disease. J. Allergy, 23:429 (Sept.) 1952.
120. Von Witzleben, H. D.: Adjunctive therapy in migraine. J. Missouri M. A., page 486 (June) 1952.
121. Waldbott, G.: Letters of Inter. Corr. Soc., Series 15, page 88.
122. Walker, D. C.: Serum neuritis secondary to tetanus antitoxin. Bull. Springer Cl., 3:3 (May) 1952.
123. Walton, C. H. A., and Elliott, G. B.: Sudden death from bronchial asthma following injection of Piromen. J. Allergy, 23:322 (July) 1952.
124. Welsh, J. B.: The effect of allergy management on growth and development of allergic children. J. Pediat., 38:571, 1951.
125. White, A. A.: Fallacy in allergy. Read by title., Regional Meeting, ACP, Chicago, Ill. (Nov. 22) 1952.
126. Wiener, A. S.: The solution of certain fundamental immunological problems by studies on Rh sensitization. Ann. Allergy, 10:535 (Sept.-Oct.) 1952.
127. Wilson, L.: Protein shock from intravenous ACTH. Lancet, 2:478, 1951.
128. Wittich, F. W.: Prophylactic treatment of some types of headache. Ann. Allergy, 10:620 (Sept.-Oct.) 1952.
129. Zanfagna, P. E.: Treatment of migraine. Post-Grad. M. J., 11:423 (May) 1952.
130. Zeligman, I.: Allergic contact dermatitis due to pork corticotropin. J.A.M.A., 149:625 (May 17) 1952.

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